CHAPTER 7

MODEL FOR TUMOUR INVASION AND METASTASIS

7.1 Introduction

The development of a primary solid tumour begins with a single normal cell becoming transformed as a result of mutations in certain key genes. This transformed cell differs from a normal one in several ways, one of the most notable being its escape from the body's homeostatic mechanisms, leading to inappropriate proliferation. An individual tumour cell has the potential, over successive divisions to develop into a cluster (or nodule) of tumour cells. Further growth and proliferation leads to the development of an avascular tumour consisting of approximately 10^6 cells. This cannot grow any further, owing to its dependence on diffusion as the only means of receiving nutrients and removing waste products. For any further development to occur the tumour must initiate angiogenesis – the recruitment of blood vessels. The tumour cells first secrete angiogenic factors which in turn induce endothelial cells in a neighbouring blood vessel to degrade their basal lamina and begin to migrate towards the tumour. As it migrates, the endothelium begins to form sprouts which can then form loops and branches through which blood circulates. From these branches more sprouts form and the whole process repeats forming a capillary network which eventually connects with the tumour, completing angiogenesis and supplying the tumour with the nutrients it needs to grow further. There is now also the possibility of tumour cells finding their way into the circulation and being deposited in distant sites in the body, resulting in metastasis. The complete process of metastasis involves several sequential steps, each of which must be successfully completed by cells of the primary tumour before a secondary tumour (a metastasis) is formed. A crucial part of the invasive /metastatic process is the ability of the cancer cells to degrade the surrounding tissue or extracellular matrix (ECM) (Liotta et al, 1983; Lawrence & Steeg, 1996). This is a complex mixture of macromolecules, some of which like the collagens are believed to play a structural role and others such as laminin, fibronectin and vitronectin are important for cell adhesion, spreading and motility. We note that all of these macromolecules are bound within the tissue i.e. they are non-diffusible. The ECM can also sequester growth factors and itself be degraded to release fragments which can have growth-promoting activity. Thus, while ECM may have to be physically removed in order to allow a tumour to spread or intra or extravasate, its degradation may in addition have biological effects on tumour cells. In this chapter, we introduced a tumour invasion and metastasis model which include tumour cells, extra cellular matrix (ECM) and matrix degradation enzyme (MDM). This is extended model from the previous angiogenesis model.

7.2 Mathematical background

The model presented in this chapter is a continuum, deterministic model (based on a system of reaction-diffusion-chemotaxis equation). We choose to focus on three key variables involved in tumour cell invasion, namely: tumour cells (denoted by n), ECM (denoted by f) and MDE (denoted by m). Each of the three variables is a function of the spatial variable x and time t.

The conservation equation for the tumour cell density *n* is

$$\frac{\partial n}{\partial t} + \nabla.\left(J_{rand} + J_{hapto}\right) = 0 \qquad (7.1)$$

where $J_{hapto} = \chi n \nabla f$ is the haptotactic flux with $\chi > 0$ is the haptotactic coefficient and $J_{random} = -D\left(f, m\right)\nabla n$ is the random motility flux.

Hence, the partial differential equation governing tumour cell motion (in the absence of cell proliferation) is,

$$\frac{\partial n}{\partial t} = \nabla.\left(D\left(f, m\right)\nabla n\right) - \chi \nabla.\left(n \nabla f\right) \qquad (7.2)$$

The ECM contains many macromolecules including fibronectin, laminin and collagen which can be degraded by matrix-degrading enzymes (MDEs) (Chambers & Matrisian, 1997). We assume that the MDEs degrade ECM upon contact and hence the degradation process is modelled by,

$$\frac{\partial f}{\partial t} = -\delta m f \qquad (7.3)$$

where δ is a positive constant.

Active MDEs are produced by the tumour cells, diffuse throughout the tissue and undergo decay. The equation governing the evolution of MDE concentration is given by:

$$\frac{\partial m}{\partial t} = D_m \nabla^2 m + g(n,m) - h(n,m,f) \tag{7.4}$$

where D_m is a positive constant. g is a function the production of active MDE and h is the function the MDE decay. For simplicity, we assume that there is a linear relationship between the density of tumour cells and the level of active MDE in the surrounding tissues. So these functions were taken to be:

$g = \mu n$ (MDE production by tumour cells)

$h = \lambda m$ (natural decay)

Hence, the complete system of equations describing the interactions of the tumour cells, ECM and MDEs is given by

$$\begin{aligned}
\frac{\partial n}{\partial t} &= D_n \nabla^2 n - \chi \nabla.(n \nabla f) \\
\frac{\partial f}{\partial t} &= -\delta m f \\
\frac{\partial m}{\partial t} &= D_m \nabla^2 m + \mu n - \lambda m
\end{aligned} \tag{7.5}$$

Non-dimensionalise Eq. (7.5) by setting

$$\tilde{n} = \frac{n}{n_o}, \qquad \tilde{f} = \frac{f}{f_o}, \qquad \tilde{m} = \frac{m}{m_o}, \qquad \tilde{x} = \frac{x}{L}, \qquad \tilde{t} = \frac{t}{\tau}$$

and dropping the tildes for notational convenience, we obtain the scaled system of equations:

$$\frac{\partial n}{\partial t} = d_n \nabla^2 n - \gamma \nabla . (n \nabla f) \qquad (7.6)$$

$$\frac{\partial f}{\partial t} = -\eta m f \qquad (7.7)$$

$$\frac{\partial m}{\partial t} = d_m \nabla^2 m + \alpha n - \beta m \qquad (7.8)$$

where $d_n = \frac{D_n}{D}$, $\gamma = \frac{\chi f_o}{D}$, $\eta = \tau m_o \delta$, $d_m = \frac{D_m}{D}$, $\alpha = \frac{\tau \mu n_o}{m_o}$ and $\beta = \tau \lambda$. The initial conditions are:

$$n(x,0) = \exp\left(-\frac{x^2}{\varepsilon}\right) \qquad (7.9)$$

$$f(x,0) = 1 - 0.5 \exp\left(-\frac{x^2}{\varepsilon}\right) \qquad (7.10)$$

$$m(x,0) = 0.5 \exp\left(-\frac{x^2}{\varepsilon}\right) \qquad (7.11)$$

The approximate solutions of Eqs. (7.6-7.8) are obtained by integrating each Eqs. (7.6-7.8) once with respect to t and using the initial condition. Hence we obtained:

$$n(x,t) = n(x) + dn\int_0^t \frac{\partial^2 n}{\partial x^2}dt - \gamma\int_0^t \frac{\partial n}{\partial x}.\frac{\partial f}{\partial x}dt - \gamma\int_0^t n\frac{\partial^2 f}{\partial x^2}dt \tag{7.12}$$

$$f(x,t) = f(x) - \eta\int_0^t mfdt \tag{7.13}$$

$$m(x,t) = m(x) + dm\int_0^t \frac{\partial^2 m}{\partial x^2}dt + \alpha\int_0^t ndt - \beta\int_0^t mdt \tag{7.14}$$

In Eqs. (7.12-7.14), we assume $n(x), f(x)$ and $m(x)$ are bounded for all x in $J = [0,T], (T \in \Re)$ and $|t-\tau| \le m', \forall 0 \le t, \tau \le T$. The terms $\frac{\partial^2 n}{\partial x^2}, \frac{\partial n}{\partial x}.\frac{\partial f}{\partial x}, n\frac{\partial^2 f}{\partial x^2}, F_1(mf) = mf, \frac{\partial^2 m}{\partial x^2}, F_2(n) = n$ and $F_3(m) = m$ are Lipschitz continuous with

$$\left|\frac{\partial^2 n}{\partial x^2} - \frac{\partial^2 n^*}{\partial x^2}\right| \le L_1|n - n^*|,$$

$$\left|\frac{\partial n}{\partial x}.\frac{\partial f}{\partial x} - \frac{\partial n^*}{\partial x}.\frac{\partial f^*}{\partial x}\right| \le L_2|nf - n^* f^*|,$$

$$\left|n\frac{\partial^2 f}{\partial x^2} - n^*\frac{\partial^2 f^*}{\partial x^2}\right| \le L_3|nf - n^* f^*|,$$

$$|F_1(m, f) - F_1(m^*, f^*)| \le L_4|mf - mf^*|,$$

$$\left|\frac{\partial^2 m}{\partial x^2} - \frac{\partial^2 m^*}{\partial x^2}\right| \le L_5|m - m^*|,$$

$$|F_2(n) - F_2(n^*)| \le L_6|n - n^*|,$$

$$\left|F_3(m) - F_3(m^*)\right| \le L_7 \left|m - m^*\right|$$

and

$$\alpha = T\left(m' L_1 + m' L_2 + m' L_3 + m' L_4 + m' L_5 + m' L_6 + m' L_7\right)$$

$$\beta = 1 - T(1 - \alpha) \tag{7.15}$$

7.3. Adomian Decomposition Method (ADM)

The Adomian decomposition method is applied in Eqs. (7.6 – 7.8):

$$L_t n = d_n \frac{\partial^2 n}{\partial x^2} - \gamma\left[\frac{\partial n}{\partial x}\frac{\partial f}{\partial x} + n\frac{\partial^2 f}{\partial x^2}\right] \tag{7.16}$$

$$L_t f = -\eta m f \tag{7.17}$$

$$L_t m = d_m \frac{\partial^2 m}{\partial x^2} + \alpha n - \beta m \tag{7.18}$$

where $L_t = \frac{\partial}{\partial t}$ is integrable differential operator with $L_t^{-1} = \int_0^t (.) dt$.

Operating on both sides of Eqs. (7.16 – 7.18) with the integral operator L^{-1} lead to

$$n(x,t) = n(x,0) + d_n L_t^{-1}\left(\frac{\partial^2 n}{\partial x^2}\right) - \gamma\left[L_t^{-1}\left[N_1(n, f)\right] + L_t^{-1}\left[N_2(n, f)\right]\right] \tag{7.19}$$

$$f(x,t) = f(x,0) - \eta L_t^{-1}\left[N_3(m, f)\right] \tag{7.20}$$

$$m(x,t) = m(x,0) + L_t^{-1}\left(d_m \frac{\partial^2 m}{\partial x^2}\right) + L_t^{-1}[\alpha n - \beta m] \tag{7.21}$$

where $$N_1(n, f) = \frac{\partial n}{\partial x}\frac{\partial f}{\partial x} \tag{7.22}$$

$$N_2(n, f) = n\frac{\partial^2 f}{\partial x^2} \tag{7.23}$$

$$N_3(m, f) = mf \tag{7.24}$$

are the nonlinear terms. The solutions $n(x,t)$, $f(x,t)$ and $m(x,t)$ can be decomposed by an infinite series as follows (Adomian, 1994):

$$n(x,t) = \sum_{i=0}^{\infty} n_i(x,t) \tag{7.25}$$

$$f(x,t) = \sum_{i=0}^{\infty} f_i(x,t) \tag{7.26}$$

$$m(x,t) = \sum_{i=0}^{\infty} m_i(x,t) \tag{7.27}$$

where $n_i(x,t)$, $f_i(x,t)$ and $m_i(x,t)$ are the components of $n(x,t)$, $f(x,t)$ and $m(x,t)$ that will elegantly determined. The nonlinear term $N(x,t)$ is decomposed by the following infinite series:

$$N_k(x,t) = \sum_{l=0}^{\infty} A_{kl} \quad , \quad k=1,2,3 \tag{7.28}$$

where A_{kl} is called Adomian's polynomial and define by:

$$A_{kl} = \frac{1}{l!}\left[\frac{d^l}{d\lambda^l} N_k\left(\sum_{i=0}^{\infty}\lambda^i n_i, \sum_{i=0}^{\infty}\lambda^i f_i, \sum_{i=0}^{\infty}\lambda^i m_i\right)\right]_{\lambda=0}, \quad i \geq 0 \tag{7.29}$$

From the above consideration, the decomposition method defines the components $n_i(x,t)$, $f_i(x,t)$ and $m_i(x,t)$ for $i \geq 0$ by the following recursive relationships:

For $n_i(x,t)$

$$n_0(x,t) = n(x,0)$$

$$n_{l+1}(x,t) = \int_0^t \left[d_n \frac{\partial^2 n_l}{\partial x^2} - \gamma\{A_{1,l}(n, f) + A_{2,l}(n, f)\}\right] d\tau, \quad l \geq 0 \tag{7.30}$$

For $f(x,t)$,

$$f_0(x,t) = f(x,0)$$

$$f_{l+1}(x,t) = -\eta \int_0^t [A_{3,l}(m, f)] d\tau, \quad l \geq 0 \tag{7.31}$$

For $m_i(x,t)$,

$$m_0(x,t) = m(x,0)$$

$$m_{l+1}(x,t) = \int_0^t \left[d_m \frac{\partial^2 m_l}{\partial x^2} + \alpha n_l - \beta m_l\right] d\tau, \quad l \geq 0 \tag{7.32}$$

7.4 Homotopy Perturbation Method (HPM)

To solve Eqs. (7.6 – 7.8) with the HPM method, we construct the following homotopy:

$$H_1(n, f, p) = (1-p)\left(\frac{\partial n}{\partial t} - \frac{\partial n_0}{\partial t}\right) + p\left(\frac{\partial n}{\partial t} - d_n \frac{\partial^2 n}{\partial x^2} + \gamma \frac{\partial n}{\partial x}.\frac{\partial f}{\partial x} + \gamma n \frac{\partial^2 f}{\partial x^2}\right) = 0 \tag{7.33}$$

$$H_2(f, m, p) = (1-p)\left(\frac{\partial f}{\partial t} - \frac{\partial f_0}{\partial t}\right) + p\left(\frac{\partial f}{\partial t} + \eta m f\right) = 0 \tag{7.34}$$

$$H_3(m, n, p) = (1-p)\left(\frac{\partial m}{\partial t} - \frac{\partial m_0}{\partial t}\right) + p\left(\frac{\partial m}{\partial t} - d_m \frac{\partial^2 m}{\partial x^2} - \alpha n + \beta m\right) = 0 \tag{7.35}$$

or

$$H_1(n, f, p) = \frac{\partial n}{\partial t} - \frac{\partial n_0}{\partial t} + p\left(-d_n \frac{\partial^2 n}{\partial x^2} + \gamma \frac{\partial n}{\partial x}.\frac{\partial f}{\partial x} + \gamma n \frac{\partial^2 f}{\partial x^2} + \frac{\partial n_o}{\partial t}\right) = 0 \tag{7.36}$$

$$H_2(f, m, p) = \frac{\partial f}{\partial t} - \frac{\partial f_0}{\partial t} + p\left(\eta m f + \frac{\partial f_0}{\partial t}\right) = 0 \tag{7.37}$$

$$H_3(m, n, p) = \frac{\partial m}{\partial t} - \frac{\partial m_0}{\partial t} + p\left(-d_m \frac{\partial^2 m}{\partial x^2} - \alpha n + \beta m + \frac{\partial m_0}{\partial t}\right) = 0 \tag{7.38}$$

In HPM, the solution of Eqs. (7.36 – 7.38) are expressed as power series in *p*;

$$n(x,t) = n_o(x,t) + p n_1(x,t) + p^2 n_2(x,t) + p^3 n_3(x,t) + \ldots \tag{7.39}$$

$$f(x,t) = f_o(x,t) + p f_1(x,t) + p^2 f_2(x,t) + p^3 f_3(x,t) + \ldots \tag{7.40}$$

$$m(x,t) = m_o(x,t) + p m_1(x,t) + p^2 m_2(x,t) + p^3 m_3(x,t) + \ldots \tag{7.41}$$

where $p \in [0,1]$ is an embedding parameter and n_o, f_o and m_o the arbitrary initial approximation satisfying the given initial condition. As p approaching to 1, we obtained

$$n(x,t) = \lim_{p \to 1} n = n_0 + n_1 + n_2 + n_3 + ... = \sum_{i=0}^{\infty} n_i \tag{7.42}$$

$$f(x,t) = \lim_{p \to 1} f = f_0 + f_1 + f_2 + f_3 + ... = \sum_{i=0}^{\infty} f_i \tag{7.43}$$

$$m(x,t) = \lim_{p \to 1} m = m_0 + m_1 + m_2 + m_3 + ... = \sum_{i=0}^{\infty} m_i \tag{7.44}$$

Substituting Eqs. (7.42 – 7.43) into Eq. (7.36):

$$\begin{aligned}
&\frac{\partial}{\partial t}\left(n_0 + pn_1 + p^2 n_2 + p^3 n_3 + ...\right) - \frac{\partial n_0}{\partial t} + p\Bigg[-d_n \frac{\partial^2}{\partial x^2}\left(n_0 + pn_1 + p^2 n_2 + p^3 n_3 + ...\right) \\
&+ \gamma \frac{\partial}{\partial x}\left(n_0 + pn_1 + p^2 n_2 + p^3 n_3 + ...\right)\frac{\partial}{\partial x}\left(f_0 + pf_1 + p^2 f_2 + p^3 f_3 + ...\right) \\
&+ \gamma\left(n_0 + pn_1 + p^2 n_2 + p^3 n_3 + ...\right)\frac{\partial^2}{\partial x^2}\left(f_0 + pf_1 + p^2 f_2 + p^3 f_3 + ...\right) + \frac{\partial n_0}{\partial t}\Bigg] = 0
\end{aligned} \tag{7.45}$$

Substituting Eqs. (7.43 – 7.44) into Eq. (7.37):

$$\begin{aligned}
&\frac{\partial}{\partial t}\left(f_0 + pf_1 + p^2 f_2 + p^3 f_3 + ...\right) - \frac{\partial f_0}{\partial t} + \\
&p\left[\eta\left(m_0 + pm_1 + p^2 m_2 + p^3 m_3 + ...\right)\left(f_0 + pf_1 + p^2 f_2 + p^3 f_3 + ...\right) + \frac{\partial f_0}{\partial t}\right] = 0
\end{aligned} \tag{7.46}$$

Substituting Eqs. (7.42 - 7.44) into Eq. (7.38):

$$\frac{\partial}{\partial t}\left(m_0 + pm_1 + p^2m_2 + p^3m_3 + ...\right) - \frac{\partial m_0}{\partial t} + p\left[-d_m \frac{\partial^2}{\partial x^2}\left(m_0 + pm_1 + p^2m_2 + p^3m_3 + ...\right)\right.$$
$$\left. - \alpha\left(n_0 + pn_1 + p^2n_2 + p^3n_3 + ...\right) + \beta\left(m_0 + pm_1 + p^2m_2 + p^3m_3 + ...\right) + \frac{\partial m_0}{\partial t}\right] = 0$$

(7.47)

Equating the coefficients of the terms in Eqs. (7.45 – 7.47) with the identical powers of *p*, we obtained:

From Eq. (7.45):

$$p^o : \frac{\partial n_0}{\partial t} - \frac{\partial n_0}{\partial t} = 0$$

$$p^1 : \frac{\partial n_1}{\partial t} - d_n \frac{\partial^2 n_0}{\partial x^2} + \gamma \frac{\partial n_0}{\partial x}\frac{\partial f_0}{\partial x} + \gamma n_0 \frac{\partial^2 f_0}{\partial x^2} + \frac{\partial n_0}{\partial t} = 0$$

$$p^2 : \frac{\partial n_2}{\partial t} - d_n \frac{\partial^2 n_1}{\partial x^2} + \gamma \frac{\partial n_0}{\partial x}\frac{\partial f_1}{\partial x} + \gamma \frac{\partial n_1}{\partial x}\frac{\partial f_0}{\partial x} + \gamma n_0 \frac{\partial^2 f_1}{\partial x^2} + \gamma n_1 \frac{\partial^2 f_0}{\partial x^2} = 0 \qquad (7.48)$$

$$p^3 : \frac{\partial n_3}{\partial t} - d_n \frac{\partial^2 n_2}{\partial x^2} + \gamma \frac{\partial n_0}{\partial x}\frac{\partial f_2}{\partial x} + \gamma \frac{\partial n_1}{\partial x}\frac{\partial f_1}{\partial x} + \gamma \frac{\partial n_2}{\partial x}\frac{\partial f_0}{\partial x} + \gamma n_0 \frac{\partial^2 f_2}{\partial x^2} + \gamma n_1 \frac{\partial^2 f_1}{\partial x^2} + \gamma n_2 \frac{\partial^2 f_0}{\partial x^2} = 0$$

$$p^4 : \frac{\partial n_4}{\partial t} - d_n \frac{\partial^2 n_3}{\partial x^2} + \gamma \frac{\partial n_0}{\partial x}\frac{\partial f_3}{\partial x} + \gamma \frac{\partial n_1}{\partial x}\frac{\partial f_2}{\partial x} + \gamma \frac{\partial n_2}{\partial x}\frac{\partial f_1}{\partial x} + \gamma \frac{\partial n_3}{\partial x}\frac{\partial f_0}{\partial x} + \gamma n_0 \frac{\partial^2 f_3}{\partial x^2} + \gamma n_1 \frac{\partial^2 f_2}{\partial x^2} + \gamma n_2 \frac{\partial^2 f_1}{\partial x^2}$$
$$+ n_3 \frac{\partial f_0}{\partial x} = 0$$

From Eq. (7.46) :

$$p^o : \frac{\partial f_0}{\partial t} - \frac{\partial f_0}{\partial t} = 0$$

$$p^1 : \frac{\partial f_1}{\partial t} + \eta m_0 f_0 + \frac{\partial f_0}{\partial t} = 0$$

$$p^2 : \frac{\partial f_2}{\partial t} + \eta m_0 f_1 + \eta m_1 f_0 = 0 \tag{7.49}$$

$$p^3 : \frac{\partial f_3}{\partial t} + \eta m_0 f_2 + \eta m_1 f_1 + \eta m_2 f_0 = 0$$

$$p^4 : \frac{\partial f_4}{\partial t} + \eta m_0 f_3 + \eta m_1 f_2 + \eta m_2 f_1 + \eta m_3 f_0 = 0$$

From Eq. (7.47) :

$$p^o : \frac{\partial m_0}{\partial t} - \frac{\partial m_0}{\partial t} = 0$$

$$p^1 : \frac{\partial m_1}{\partial t} - d_m \frac{\partial^2 m_0}{\partial x^2} - \alpha n_0 + \beta m_0 + \frac{\partial m_0}{\partial t} = 0$$

$$p^2 : \frac{\partial m_2}{\partial t} - d_m \frac{\partial^2 m_1}{\partial x^2} - \alpha n_1 + \beta m_1 = 0 \tag{7.50}$$

$$p^3 : \frac{\partial m_3}{\partial t} - d_m \frac{\partial^2 m_2}{\partial x^2} - \alpha n_2 + \beta m_2 = 0$$

$$p^4 : \frac{\partial m_4}{\partial t} - d_m \frac{\partial^2 m_3}{\partial x^2} - \alpha n_3 + \beta m_3 = 0$$

Solving Eqs. (7.48 – 7.50), we will have the solution of Eqs. (7.6 – 7.8).

7.5 Existence and convergence of ADM and HPM

Theorem 7.1: Let $0 < \alpha < 1$, then Eqs. (7.6 - 7.8) have a unique solution.

Proof:

(I) Let n and n^* be two different solutions of Eq. (7.12) then

$$\left|n-n^*\right| = \left|\begin{array}{l} dn\int_0^t \left[\frac{\partial^2 n}{\partial x^2}-\frac{\partial^2 n^*}{\partial x^2}\right]dt - \gamma\int_0^t \left(\frac{\partial n}{\partial x}.\frac{\partial f}{\partial x}-\frac{\partial n*}{\partial x}.\frac{\partial f*}{\partial x}\right)dt \\ -\gamma\int_0^t \left(n\frac{\partial^2 f}{\partial x^2}-n*\frac{\partial^2 f*}{\partial x^2}\right)dt \end{array}\right|$$

$$\leq |dn|\int_0^t \left|\left[\frac{\partial^2 n}{\partial x^2}-\frac{\partial^2 n*}{\partial x^2}\right]\right|dt + |\gamma|\int_0^t \left|\frac{\partial n}{\partial x}.\frac{\partial f}{\partial x}-\frac{\partial n*}{\partial x}.\frac{\partial f*}{\partial x}\right|dt + |\gamma|\int_0^t \left|n\frac{\partial^2 f}{\partial x^2}-n*\frac{\partial^2 f*}{\partial x^2}\right|dt$$

$$\leq T\left(m' L_1 + m' L_2 + m' L_3\right)|n-n*|$$

$$=\alpha|n-n*|$$

From which we get $(1-\alpha)|n-n*|\leq 0$. Since $0<\alpha<1$, then $|n-n*|=0$. Implies $n=n*$ and completes the proof.

(II) Let f and f^* be two different solutions of Eq. (7.13) then

$$\left|f-f^*\right| = \left|-\eta\int_0^t \left(F_1(mf)-F_1(m*f*)\right)dz\right|$$

$$\leq |\eta|\left|\int_0^t \left(F_1(mf)-F_1(m*f*)\right)dz\right|$$

$$\leq T\left(m' L_4\right)$$

$$=\alpha|f-f*|$$

From which we get $(1-\alpha)|f - f*| \le 0$. Since $0 < \alpha < 1$, then $|f - f*| = 0$. Implies $f = f*$ and completes the proof.

(III) Let m and m^* be two different solutions of Eq. (7.14) then

$$|m - m^*| = \left| \begin{array}{l} dm\int_0^t \left[\frac{\partial^2 m}{\partial x^2} - \frac{\partial^2 m^*}{\partial x^2} \right] dt + \gamma \int_0^t \left(F_2(n) - F_2(n^*) \right) dt \\ - \beta \int_0^t \left(F_3(m) - F_3(m^*) \right) dt \end{array} \right|$$

$$\le |dm| \int_0^t \left| \left[\frac{\partial^2 m}{\partial x^2} - \frac{\partial^2 m*}{\partial x^2} \right] \right| dt + |\alpha| \int_0^t |F_2(n) - F_2(n*)| dt + |\beta| \int_0^t |F_4(n) - F_4(n*)| dt$$

$$\le T(m' L_5 + m' L_6 + m' L_7)|m - m^*|$$

$$= \alpha |m - m*|$$

From which we get $(1-\alpha)|m - m*| \le 0$. Since $0 < \alpha < 1$, then $|m - m*| = 0$. Implies $m = m*$ and completes the proof.

Theorem 7.2: The series solution $n(x,t) = \sum_{i=0}^{\infty} n_i(x,t)$, $f(x,t) = \sum_{i=0}^{\infty} f_i(x,t)$ and $m(x,t) = \sum_{i=0}^{\infty} m_i(x,t)$ of Eqs. (7.16 – 7.18), respectively using ADM converges if $0 < \alpha < 1$, , $|n_1(x,t)| < \infty$, $|f_1(x,t)| < \infty$, $|m_1(x,t)| < \infty$.

Proof: Denote as $(C[J],\|.\|)$ the Banach space of all continuous functions on J with the norm $\|f(t)\| = \max \forall_t \in J$. Define the sequence of partial series $\{S_n\}$; Let S_n and S_m be arbitrary partial sums with $n \geq m$. We prove that S_n is a Cauchy sequence in this Banach space:

(I) For Eq. (7.16)

$$\|S_n - S_m\| = \max_{\forall t \in J} |S_n - S_m|$$

$$= \max_{\forall t \in J} \left| \sum_{i=k+1}^{n} n_i(x,t) \right|$$

$$= \max_{\forall t \in J} \left| \sum_{i=k+1}^{n} \left(\int_0^t dn \frac{\partial^2 n_i}{\partial x^2} dt - \gamma \int_0^t \frac{\partial n}{\partial x} . \frac{\partial f}{\partial x} dt - \gamma \int_0^t n \frac{\partial^2 f}{\partial x^2} dt \right) \right|$$

$$= \max_{\forall t \in J} \left| dn \int_0^t \left(\sum_{i=k}^{n-1} \frac{\partial^2 n_i}{\partial x^2} \right) dt - \gamma \int_0^t \left(\sum_{i=k}^{n-1} \frac{\partial n_i}{\partial x} . \frac{\partial f_i}{\partial x} \right) dt - \gamma \int_0^t \left(\sum_{i=k}^{n-1} n_i \frac{\partial^2 f_i}{\partial x^2} \right) dt \right|$$

From Kalla (2008), we have

$$\sum_{i=k}^{n-1} \frac{\partial^2 n_i}{\partial x^2} = G_1^{\,2}(S_{n-1}) - G_1^{\,2}(S_{m-1})$$

$$\sum_{i=k}^{n-1} \frac{\partial\ n_i}{\partial x} . \frac{\partial f_i}{\partial x} = G_2^{\,2}(S_{n-1}) - G_2^{\,2}(S_{m-1})$$

$$\sum_{i=k}^{n-1} n_i \frac{\partial^2 f_i}{\partial x^2} = G_3^{\,2}(S_{n-1}) - G_3^{\,2}(S_{m-1})$$

So

$$\|S_n - S_m\| = \max_{\forall t \in J}\left| dn\int_0^t \left[G_1{}^2(S_{n-1}) - G_1{}^2(S_{m-1})\right]dt - \gamma\int_0^t \left[G_2{}^2(S_{n-1}) - G_2{}^2(S_{m-1})\right]dt - \gamma\int_0^t \left[G_3{}^2(S_{n-1}) - G_3{}^2(S_{m-1})\right]dt \right|$$

$$\leq |dn|\int_0^t \left|G_1{}^2(S_{n-1}) - G_1{}^2(S_{m-1})\right|dt + |\gamma|\int_0^t \left|G_2{}^2(S_{n-1}) - G_2{}^2(S_{m-1})\right|dt + |\gamma|\int_0^t \left|G_3{}^2(S_{n-1}) - G_3{}^2(S_{m-1})\right|dt$$

$$\leq \alpha\|S_n - S_m\| \qquad (7.51)$$

(I) For Eq. (7.17)

$$\|S_n - S_m\| = \max_{\forall t \in J}|S_n - S_m|$$

$$= \max_{\forall t \in J}\left|\sum_{i=k+1}^{n} f_i(x,t)\right|$$

$$= \max_{\forall t \in J}\left|\sum_{i=k+1}^{n}\left(-\eta\int_0^t m_i f_i dt\right)\right|$$

$$= \max_{\forall t \in J}\left|-\eta\int_0^t\left(\sum_{i=k}^{n-1} m_i f_i\right)dt\right|$$

From Kalla (2008), we have

$$\sum_{i=k}^{n-1} m_i f_i = F_1(S_{n-1}) - F_1(S_{m-1})$$

So

$$\|S_n - S_m\| = \max_{\forall t \in J}\left|-\eta\int_0^t \left[F_1(S_{n-1}) - F_1(S_{m-1})\right]dt\right|$$

$$\leq |\eta| \int_0^t |F_1(S_{n-1}) - F_1(S_{m-1})| dt$$

$$\leq \alpha \| S_n - S_m \| \tag{7.52}$$

(II) For Eq. (7.18)

$$\| S_n - S_m \| = \max_{\forall t \in J} | S_n - S_m |$$

$$= \max_{\forall t \in J} \left| \sum_{i=k+1}^{n} m_i(x,t) \right|$$

$$= \max_{\forall t \in J} \left| \sum_{i=k+1}^{n} \left(\int_0^t dm \frac{\partial^2 m_i}{\partial x^2} dt + \alpha \int_0^t n_i dz - \beta \int_0^t m_i dt \right) \right|$$

$$= \max_{\forall t \in J} \left| dm \int_0^t \left(\sum_{i=k}^{n-1} \frac{\partial^2 m_i}{\partial x^2} \right) dt + \alpha \int_0^t \left(\sum_{i=k}^{n-1} n_i \right) dt - \beta \int_0^t \left(\sum_{i=k}^{n-1} m_i \right) dt \right|$$

From Kalla (2008), we have

$$\sum_{i=k}^{n-1} \frac{\partial^2 m_i}{\partial x^2} = G_4{}^2(S_{n-1}) - G_4{}^2(S_{m-1})$$

$$\sum_{i=k}^{n-1} n_i = F_2(S_{n-1}) - F_2(S_{m-1})$$

$$\sum_{i=k}^{n-1} m_i = F_3(S_{n-1}) - F_3(S_{m-1})$$

So

$$\|S_n - S_m\| = \max_{\forall t\in J}\left| dm\int_0^t \left[G_4{}^2(S_{n-1}) - G_4{}^2(S_{m-1})\right]dt + \alpha\int_0^t \left[F_2(S_{n-1}) - F_2(S_{m-1})\right]dt - \beta\int_0^t \left[F_3(S_{n-1}) - F_3(S_{m-1})\right]dt \right|$$

$$\le |dm|\int_0^t \left|G_4{}^2(S_{n-1}) - G_4{}^2(S_{m-1})\right|dt + |\alpha|\int_0^t \left|F_2(S_{n-1}) - F_2(S_{m-1})\right|dt + |\beta|\int_0^t \left|F_3(S_{n-1}) - F_3(S_{m-1})\right|dt$$

$$\le \alpha\|S_n - S_m\| \tag{7.53}$$

For Eq. (7.51), let $n = m + 1$, then

$$\|S_{m+1} - S_m\| \le \alpha\|S_m - S_{m-1}\|$$

$$\le \alpha^2\|S_{m-1} - S_{m-2}\|$$

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$$\le \alpha^m\|S_1 - S_0\|$$

From the triangle inequality, we have

$$\|S_n - S_m\| \le \|S_{m+1} - S_m\| + \|S_{m+2} - S_{m+1}\| + \ldots.. + \|S_n - S_{n-1}\|$$

$$\le \left(\alpha^m + \alpha^{m+1} + \ldots.. + \alpha^{n-m-1}\right)\|S_1 - S_0\|$$

$$\le \alpha^m\left(1 + \alpha + \alpha^2 + \ldots.. + \alpha^{n-m-1}\right)\|S_1 - S_0\|$$

$$\leq \alpha^{m}\left(\frac{1-\alpha^{n-m}}{1-\alpha}\right)\|n_1(x,t)\|$$

Similar steps for Eq. (7.52)

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. $\leq \alpha^{m}\left(\frac{1-\alpha^{n-m}}{1-\alpha}\right)\|f_1(x,t)\|$

Similar steps for Eq. (7.53)

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$$\leq \alpha^{m}\left(\frac{1-\alpha^{n-m}}{1-\alpha}\right)\|m_1(x,t)\|$$

Since $0<\alpha<1$, we have $(1-\alpha^{n-m})<1$,

then $\|S_n - S_m\| \leq \frac{\alpha^m}{1-\alpha}\max_{\forall t\in J}|n_1(x,t)|$ (7.54)

$$\|S_n - S_m\| \leq \frac{\alpha^m}{1-\alpha}\max_{\forall t\in J}|f_1(x,t)| \quad (7.55)$$

$$\|S_n - S_m\| \leq \frac{\alpha^m}{1-\alpha}\max_{\forall t\in J}|m_1(x,t)| \quad (7.56)$$

But $|n_1(x,t), f_1(x,t), m_1(x,t)| < \infty,$ so as $m \to \infty$ then $\|S_n - S_m\| \to 0.$ We confidence that $\{S_n\}$ is a Cauchy sequence in $C[J]$, therefore the series is converges and the proof is completed.

Theorem 7.3: If $|n_m(x,t)| \le 1,$ $|f_m(x,t)| \le 1,$ $|m_m(x,t)| \le 1,$ then the series solution $n(x,t) = \sum_{i=0}^{\infty} n_i(x,t),$ $f(x,t) = \sum_{i=0}^{\infty} f_i(x,t), m(x,t) = \sum_{i=0}^{\infty} m_i(x,t)$ of Eqs. (7.6-7.8) converges to the exact solution by using HPM.

Proof:

(I) For Eq. (7.6)

We set,

$$\phi_n(x,t) = \sum_{i=1}^{n} n_i(x,t)$$

$$\phi_{n+1}(x,t) = \sum_{i=1}^{n+1} n_i(x,t)$$

So,

$$|\phi_{n+1}(x,t) - \phi_n(x,t)| = |\phi_n + n_n - \phi_n|$$

$$= |n_n|$$

$$\le \sum_{k=0}^{m-1} (|dn| \int_0^t \left| \frac{\partial^2 n_{m-k-1}}{\partial x^2} \right| dt + |\gamma| \int_0^t | \quad \frac{\partial n_{k-m-1}}{\partial x} . \frac{\partial f_{k-m-1}}{\partial x} \quad | dt + |\gamma| \int_0^t \left| n_{k-m-1} \frac{\partial^2 f_{k-m-1}}{\partial x^2} \right|) dt$$

Thus

$$\sum_{n=0}^{\infty}\left\|\phi_{n+1}(x,t)-\phi_n(x,t)\right\| \le (m-1)\alpha\left|f(x)\right|\sum_{n=0}^{\infty}\alpha^n$$

Since $0<\alpha<1$, therefore $\lim_{n\to\infty} n_n(x,t)=n(x,t)$

(II) For Eq.(7.7)

We set,

$$\phi_n(x,t)=\sum_{i=1}^{n} f_i(x,t)$$

$$\phi_{n+1}(x,t)=\sum_{i=1}^{n+1} f_i(x,t)$$

So,

$$\left|\phi_{n+1}(x,t)-\phi_n(x,t)\right| = \left|\phi_n + f_n - \phi_n\right|$$

$$= \left|f_n\right|$$

$$\le \sum_{k=0}^{m-1}\left|\eta\right|\int_0^t \left|m_{k-m-1} f_{k-m-1}\right| dt$$

Thus

$$\sum_{n=0}^{\infty}\left\|\phi_{n+1}(x,t)-\phi_n(x,t)\right\| \le (m-1)\alpha\left|f(x)\right|\sum_{n=0}^{\infty}\alpha^n$$

Since $0<\alpha<1$, therefore $\lim_{n\to\infty} f_n(x,t)=f(x,t)$

(III) For Eq.(7.8)

We set,

$$\phi_n(x,t) = \sum_{i=1}^{n} m_i(x,t)$$

$$\phi_{n+1}(x,t) = \sum_{i=1}^{n+1} m_i(x,t)$$

So,

$$|\phi_{n+1}(x,t) - \phi_n(x,t)| = |\phi_n + m_n - \phi_n|$$

$$= |m_n|$$

$$\leq \sum_{k=0}^{m-1} (|dm| \int_0^t \left| \frac{\partial^2 m_{m-k-1}}{\partial x^2} \right| dt + |\alpha| \int_0^t |n_{k-m-1} \; |dt + |\beta| \int_0^t |m_{k-m-1}|) dt$$

Thus

$$\sum_{n=0}^{\infty} \|\phi_{n+1}(x,t) - \phi_n(x,t)\| \leq (m-1)\alpha |f(x)| \sum_{n=0}^{\infty} \alpha^n$$

Since $0 < \alpha < 1$, therefore $\lim_{n \to \infty} m_n(x,t) = m(x,t)$

7.6 Numerical experiment

In this section, we compute numerically Eqs.(7.6 – 7.8) by the ADM and HPM methods.

7.6.1 ADM method

From the ADM formula Eq.(7.29), we can obtain the first three terms of the Adomian polynomials:

$$A_{1,0} = N_1(n_0, f_0)$$

$$= \frac{\partial n_0}{\partial x}\frac{\partial f_0}{\partial x}$$

$$= -\frac{2x^2}{\varepsilon^2} e^{-\frac{2x^2}{\varepsilon}} \qquad (7.57)$$

$$A_{2,0} = N_2(n_1, f_0)$$

$$= n_0 \frac{\partial^2 f_0}{\partial x^2}$$

$$= -\frac{e^{-\frac{2x^2}{\varepsilon}}}{\varepsilon}\left(1 - \frac{2x^2}{\varepsilon}\right) \qquad (7.58)$$

$$A_{3,0} = N_3(m_0, f_0)$$

$$= (m_0 f_0)$$

$$= \frac{1}{2} e^{-\frac{x^2}{\varepsilon}}\left(1 - \frac{1}{2} e^{-\frac{x^2}{\varepsilon}}\right) \qquad (7.59)$$

By the recursive formula in Eqs. (7.30 – 7.32), we can obtain directly the components of n_i, f_i and m_i (see Appendix C)

From Eq. (7.30):

$$n_o = e^{-\frac{x^2}{\varepsilon}} \tag{7.60}$$

$$n_1 = \int_0^t \left[d_n \frac{\partial^2 n_0}{\partial x^2} - \gamma\left(A_{10} + A_{20}\right) \right] d\tau$$

$$= -\left\{ \{ 2d_n \left[1 - \frac{2x^2}{\varepsilon} \right] + \gamma e^{\frac{-x^2}{\varepsilon}} \left[1 - \frac{4x^2}{\varepsilon} \right] \right\} \frac{t}{\varepsilon} e^{\frac{-x^2}{\varepsilon}} \tag{7.61}$$

$$n_2 = -\Bigg(\Bigg\{ \Bigg\{ \frac{-4d_n}{\varepsilon} \Bigg\langle \frac{d_n}{\varepsilon} \left[3 - \frac{6x^3}{\varepsilon} - \frac{2}{\varepsilon}\left(3x^2 - \frac{2x^5}{\varepsilon} \right) \right] + e^{\frac{-x^2}{\varepsilon}} \left[\gamma\left(3 - \frac{8x^3}{\varepsilon} \right) + 3x^2 - \frac{4x^4}{\varepsilon} \right] \Bigg\} +$$

$$e^{\frac{-x^2}{\varepsilon}} \Bigg\langle \frac{2}{\varepsilon^2} \gamma\mu x^2 \left[e^{\frac{-x^2}{\varepsilon}} - 1 \right] + \frac{4x}{\varepsilon} \left\{ \frac{d_n}{\varepsilon}\left(3x - \frac{2x^3}{\varepsilon} \right) - \gamma e^{\frac{-x^2}{\varepsilon}} \left(3x - \frac{4x^3}{\varepsilon} \right) \right\}$$

$$-\gamma \frac{\mu}{\varepsilon} \left[-1 + \frac{2x^2}{\varepsilon} + e^{\frac{-x^2}{\varepsilon}} (1 - \frac{4x^2}{\varepsilon}) \right] - \gamma\left(1 - \frac{2x^2}{\varepsilon} \right) \left\{ \frac{2d_n}{\varepsilon} \left(1 - \frac{2x^2}{\varepsilon} \right) + \gamma e^{\frac{-x^2}{\varepsilon}} \left(1 - \frac{4x^2}{\varepsilon} \right) \right\} \Bigg\rangle \Bigg) \frac{t^2}{2} e^{\frac{-x^2}{\varepsilon}}$$

$$\tag{7.62}$$

From Eq. (7.31)

$$f_o = 1 - \frac{1}{2} e^{-\frac{x^2}{\varepsilon}} \tag{7.63}$$

$$f_1 = -\eta \int_0^t A_{3,0}\, d\tau$$

$$= -\left(1 - \frac{1}{2} e^{\frac{-x^2}{\varepsilon}} \right) \frac{\eta t}{2} e^{\frac{-x^2}{\varepsilon}} \tag{7.64}$$

$$f_2 = \left(1 - \frac{1}{2} e^{\frac{-x^2}{\varepsilon}} \right) \left[\frac{\eta}{4} e^{\frac{-x^2}{\varepsilon}} - \left(d_m \left(1 - 2x^2 \right) - \alpha + \frac{\beta}{2} \right) \right] \frac{\eta t^2}{2} e^{\frac{-x^2}{\varepsilon}} \tag{7.65}$$

From Eq. (7.32)

$$m_o = \frac{1}{2} e^{-\frac{x^2}{\varepsilon}} \tag{7.66}$$

$$m_1 = \int_0^t \left[d_m \frac{\partial^2 m_0}{\partial x^2} + \alpha n_0 - \beta m_0 \right] d\tau$$

$$= -\left[\frac{d_m}{\varepsilon}\left(1 - \frac{2x^2}{\varepsilon}\right) - \alpha + \frac{\beta}{2} \right] t e^{\frac{-x^2}{\varepsilon}} \tag{7.67}$$

$$m_2 = -\left(\left\{ d_m \left[-d_m \left\langle \frac{2}{\varepsilon}\left(1 - \frac{2x^2}{\varepsilon}\right) + 4\left(1 - \frac{5x^2}{\varepsilon} + \frac{2x^4}{\varepsilon^2}\right) \right\rangle + \frac{1}{\varepsilon}\left(1 - \frac{2x^2}{\varepsilon}\right)(2\alpha - \beta) \right] \right\} + \right.$$

$$\left. \alpha \left\{ \frac{2d_n}{\varepsilon}\left(1 - \frac{2x^2}{\varepsilon}\right) + \gamma e^{\frac{-x^2}{\varepsilon}} \left(1 - \frac{4x^2}{\varepsilon}\right) \right\} - \beta \left[d_m \left(1 - 2x^2\right) - \alpha + \frac{\beta}{2} \right] \right) \frac{t^2}{2} e^{\frac{-x^2}{\varepsilon}}$$

(7.68)

7.7.2 HPM method

Following the HPM method, we can obtain the first three terms of He polynomials.

From Eqs. (7.48 – 7.49):

$$n_o = e^{-\frac{x^2}{\varepsilon}} \tag{7.69}$$

$$n_1 = \int_0^t \left(d_n \frac{2}{\varepsilon} e^{\frac{-x^2}{\varepsilon}} \left[1 - \frac{2x^2}{\varepsilon} \right] + \gamma \frac{2x^2}{\varepsilon^2} e^{\frac{-x^2}{\varepsilon}} e^{\frac{-x^2}{\varepsilon}} - \gamma e^{\frac{-x^2}{\varepsilon}} e^{\frac{-x^2}{\varepsilon}} \left[1 - \frac{2x^2}{\varepsilon} \right] \right) d\tau$$

$$= -\left\{ \{ 2d_n \left[1 - \frac{2x^2}{\varepsilon} \right] + \gamma e^{\frac{-x^2}{\varepsilon}} \left[1 - \frac{4x^2}{\varepsilon} \right] \right\} \frac{t}{\varepsilon} e^{\frac{-x^2}{\varepsilon}} \tag{7.70}$$

$$n_2 = \int_0^t \Bigg(d_n \frac{4}{\varepsilon} te^{\frac{-x^2}{\varepsilon}} \left\{ \frac{d_n}{\varepsilon}\left[3 - \frac{6x^3}{\varepsilon} - \frac{2}{\varepsilon}\left(3x^2 - \frac{2x^5}{\varepsilon}\right)\right] - e^{\frac{-x^2}{\varepsilon}}\left[\gamma\left(3 - \frac{8x^3}{\varepsilon}\right) + 3x^2 - \frac{4x^4}{\varepsilon}\right]\right\} -$$

$$\frac{2}{\varepsilon}\gamma xe^{\frac{-x^2}{\varepsilon}} \frac{\mu}{\varepsilon} txe^{\frac{-x^2}{\varepsilon}}\left[-1 + e^{\frac{-x^2}{\varepsilon}}\right] - \frac{4}{\varepsilon} te^{\frac{-x^2}{\varepsilon}}\left\{\frac{d_n}{\varepsilon}\left(3x - \frac{2x^3}{\varepsilon}\right) - \gamma e^{\frac{-x^2}{\varepsilon}}\left(3x - \frac{4x^3}{\varepsilon}\right)\right\} xe^{\frac{-x^2}{\varepsilon}}$$

$$+ \gamma e^{\frac{-x^2}{\varepsilon}} \frac{\mu}{\varepsilon} te^{\frac{-x^2}{\varepsilon}}\left[-1 + \frac{2x^2}{\varepsilon} + e^{\frac{-x^2}{\varepsilon}} - \frac{4x^2}{\varepsilon} e^{\frac{-x^2}{\varepsilon}}\right] +$$

$$\gamma te^{\frac{-x^2}{\varepsilon}}\left\{\frac{2d_n}{\varepsilon}\left(1 - \frac{2x^2}{\varepsilon}\right) + \gamma e^{\frac{-x^2}{\varepsilon}}\left(1 - \frac{4x^2}{\varepsilon}\right)\right\} e^{\frac{-x^2}{\varepsilon}}\left(1 - \frac{2x^2}{\varepsilon}\right)\Bigg) d\tau$$

$$= -\Bigg(\left\{\frac{-4d_n}{\varepsilon}\left\langle\frac{d_n}{\varepsilon}\left[3 - \frac{6x^3}{\varepsilon} - \frac{2}{\varepsilon}\left(3x^2 - \frac{2x^5}{\varepsilon}\right)\right] + e^{\frac{-x^2}{\varepsilon}}\left[\gamma\left(3 - \frac{8x^3}{\varepsilon}\right) + 3x^2 - \frac{4x^4}{\varepsilon}\right]\right\} +$$

$$e^{\frac{-x^2}{\varepsilon}}\left\langle\frac{2}{\varepsilon^2}\gamma\mu x^2\left[e^{\frac{-x^2}{\varepsilon}} - 1\right] + \frac{4x}{\varepsilon}\left\{\frac{d_n}{\varepsilon}\left(3x - \frac{2x^3}{\varepsilon}\right) - \gamma e^{\frac{-x^2}{\varepsilon}}\left(3x - \frac{4x^3}{\varepsilon}\right)\right\}\right.$$

$$-\gamma\frac{\mu}{\varepsilon}\left[-1 + \frac{2x^2}{\varepsilon} + e^{\frac{-x^2}{\varepsilon}}(1 - \frac{4x^2}{\varepsilon})\right] - \gamma\left(1 - \frac{2x^2}{\varepsilon}\right)\left\{\frac{2d_n}{\varepsilon}\left(1 - \frac{2x^2}{\varepsilon}\right) + \gamma e^{\frac{-x^2}{\varepsilon}}\left(1 - \frac{4x^2}{\varepsilon}\right)\right\}\Bigg\rangle\Bigg)\frac{t^2}{2} e^{\frac{-x^2}{\varepsilon}}$$

(7.71)

From Eq. (7.49):

$$f_o = 1 - \frac{1}{2} e^{-\frac{x^2}{\varepsilon}} \tag{7.72}$$

$$f_1 = -\int_0^t \left(\frac{\eta}{2} e^{\frac{-x^2}{\varepsilon}}\left(1 - \frac{1}{2} e^{\frac{-x^2}{\varepsilon}}\right)\right) d\tau$$

$$= -\left(1 - \frac{1}{2} e^{\frac{-x^2}{\varepsilon}}\right)\frac{\eta t}{2} e^{\frac{-x^2}{\varepsilon}} \tag{7.73}$$

$$f_2 = \int_0^t \left(\eta\left[\frac{1}{2} e^{\frac{-x^2}{\varepsilon}} \frac{\eta}{2} e^{\frac{-x^2}{\varepsilon}}\left(1 - \frac{1}{2} e^{\frac{-x^2}{\varepsilon}}\right) t + e^{\frac{-x^2}{\varepsilon}}\left(d_m\left(1 - 2x^2\right) - \alpha + \frac{\beta}{2}\right) t\left(1 - \frac{1}{2} e^{\frac{-x^2}{\varepsilon}}\right)\right]\right) d\tau$$

$$=\left(1-\frac{1}{2}e^{\frac{-x^2}{\varepsilon}}\right)\left[\frac{\eta}{4}e^{\frac{-x^2}{\varepsilon}}-\left(d_m\left(1-2x^2\right)-\alpha+\frac{\beta}{2}\right)\right]\frac{\eta t^2}{2}e^{\frac{-x^2}{\varepsilon}} \quad (7.74)$$

From Eq. (7.50):

$$m_o=\frac{1}{2}e^{-\frac{x^2}{\varepsilon}} \quad (7.75)$$

$$m_1=-\int_0^t e^{\frac{-x^2}{\varepsilon}}\left[\frac{d_m}{\varepsilon}\left(1-\frac{2x^2}{\varepsilon}\right)-\alpha+\frac{\beta}{2}\right]d\tau$$

$$=-\left[\frac{d_m}{\varepsilon}\left(1-\frac{2x^2}{\varepsilon}\right)-\alpha+\frac{\beta}{2}\right]te^{\frac{-x^2}{\varepsilon}} \quad (7.76)$$

$$m_2=\int_0^t\left(-d_m te^{\frac{-x^2}{\varepsilon}}\left\{-d_m\left\langle\frac{2}{\varepsilon}\left(1-\frac{2x^2}{\varepsilon}\right)+4\left(1-\frac{5x^2}{\varepsilon}+\frac{2x^4}{\varepsilon^2}\right)\right\rangle+\frac{1}{\varepsilon}\left(1-\frac{2x^2}{\varepsilon}\right)(2\alpha-\beta)\right\}-\right.$$
$$\left.\alpha te^{\frac{-x^2}{\varepsilon}}\left\{\frac{2d_n}{\varepsilon}\left(1-\frac{2x^2}{\varepsilon}\right)+\gamma e^{\frac{-x^2}{\varepsilon}}\left(1-\frac{4x^2}{\varepsilon}\right)\right\}+\beta e^{\frac{-x^2}{\varepsilon}}t\left[d_m\left(1-2x^2\right)-\alpha+\frac{\beta}{2}\right]\right)d\tau$$

$$m_2=-\left(\left\{d_m\left[-d_m\left\langle\frac{2}{\varepsilon}\left(1-\frac{2x^2}{\varepsilon}\right)+4\left(1-\frac{5x^2}{\varepsilon}+\frac{2x^4}{\varepsilon^2}\right)\right\rangle+\frac{1}{\varepsilon}\left(1-\frac{2x^2}{\varepsilon}\right)(2\alpha-\beta)\right]\right\}+\right.$$
$$\left.\alpha\left\{\frac{2d_n}{\varepsilon}\left(1-\frac{2x^2}{\varepsilon}\right)+\gamma e^{\frac{-x^2}{\varepsilon}}\left(1-\frac{4x^2}{\varepsilon}\right)\right\}-\beta\left[d_m\left(1-2x^2\right)-\alpha+\frac{\beta}{2}\right]\right)\frac{t^2}{2}e^{\frac{-x^2}{\varepsilon}}$$

(7.77)

It is obvious that the first three terms approximate solutions (Eqs. (7.60 – 7.68)) obtained using ADM are the same as the first four terms (Eqs. (7.69 – 7.77)) of the HPM.

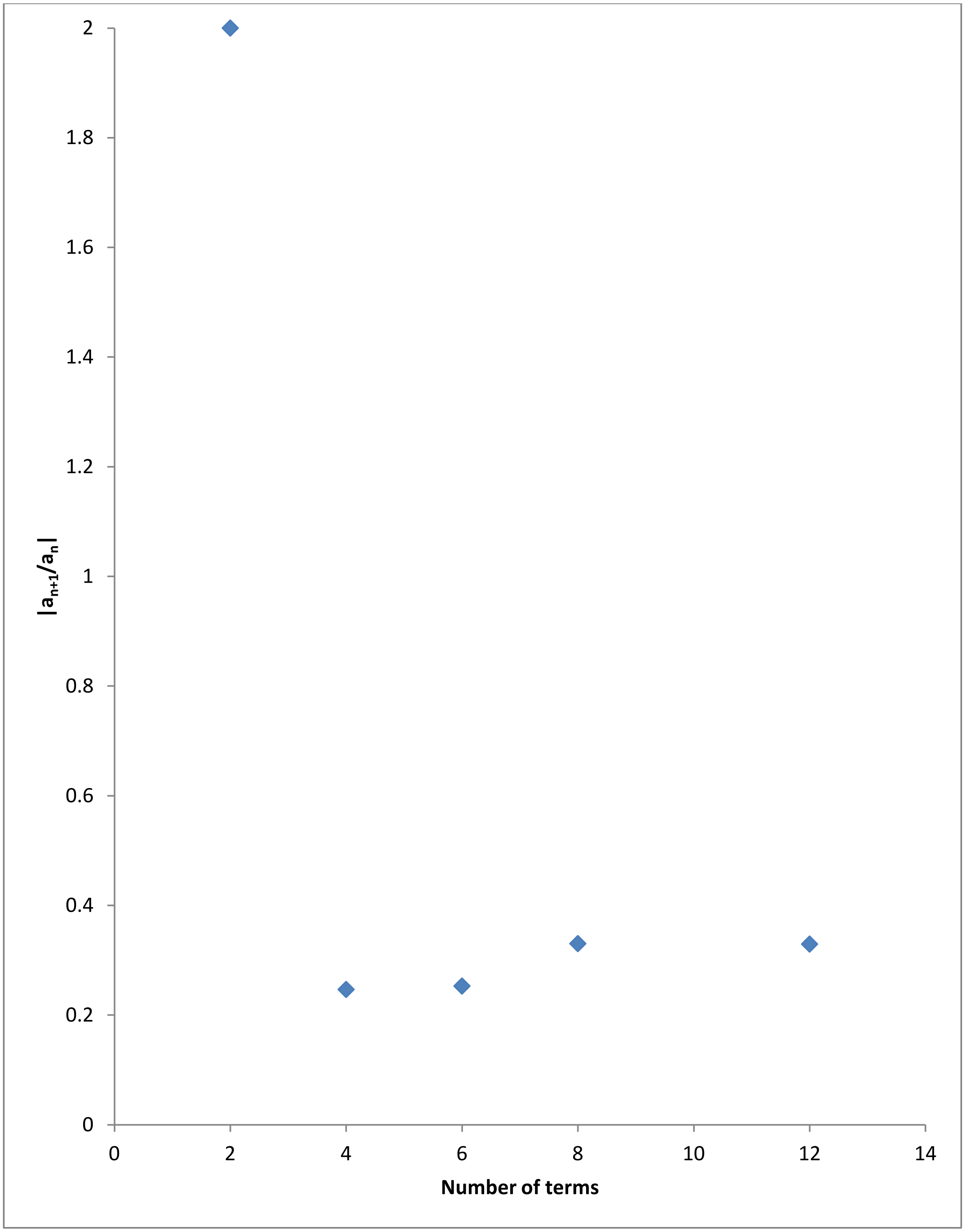
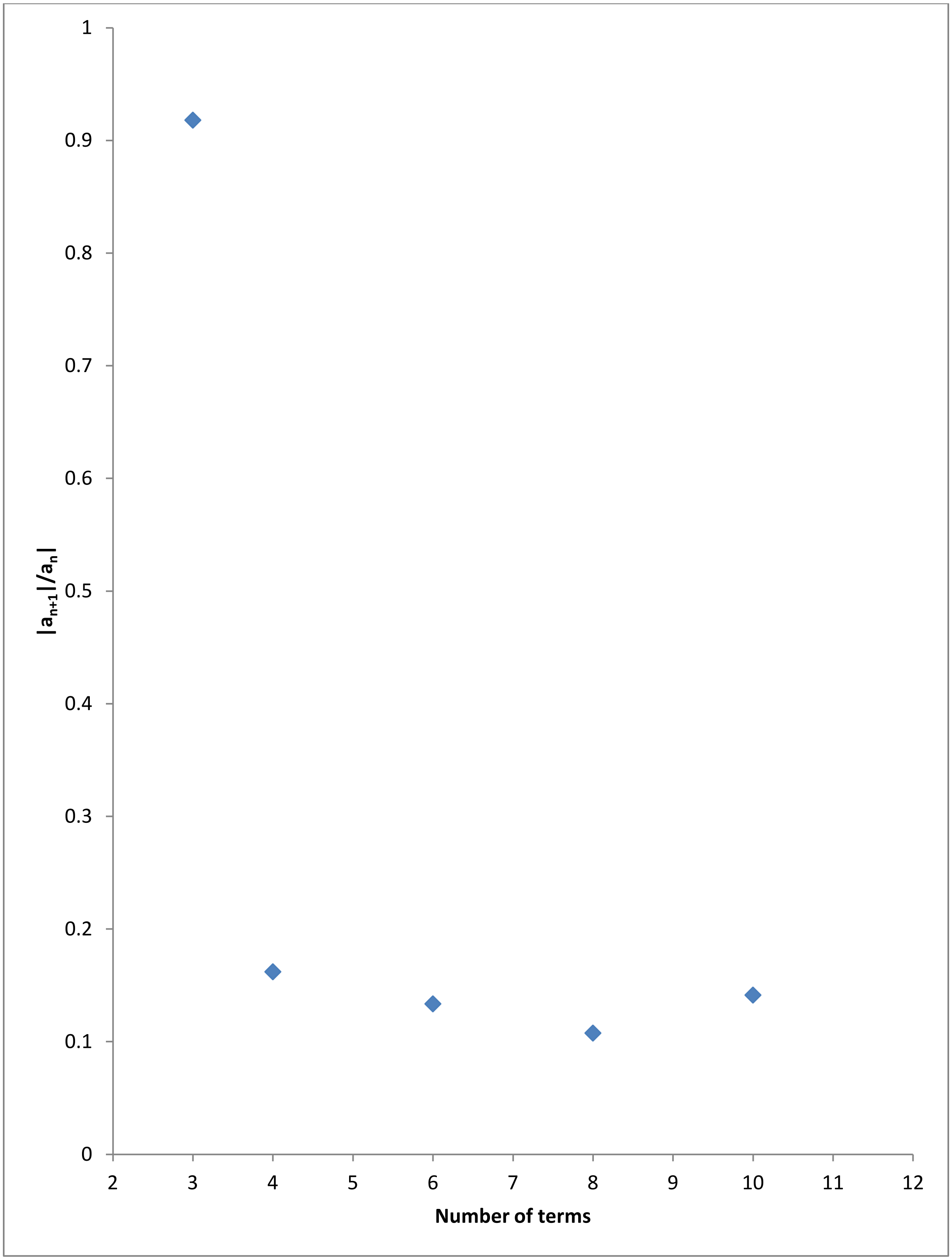


Figure 7.1. The ratio convergence test applied to the series coefficients (tumour) for ADM and HPM as a function of the number of terms in series.



1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
|a_{n+1}|/a_n|
2
3
4
5
6
7
8
9
10
11
12
Number of terms

Figure 7.2. The ratio convergence test applied to the series coefficients (ECM) for ADM and HPM as a function of the number of terms in series.

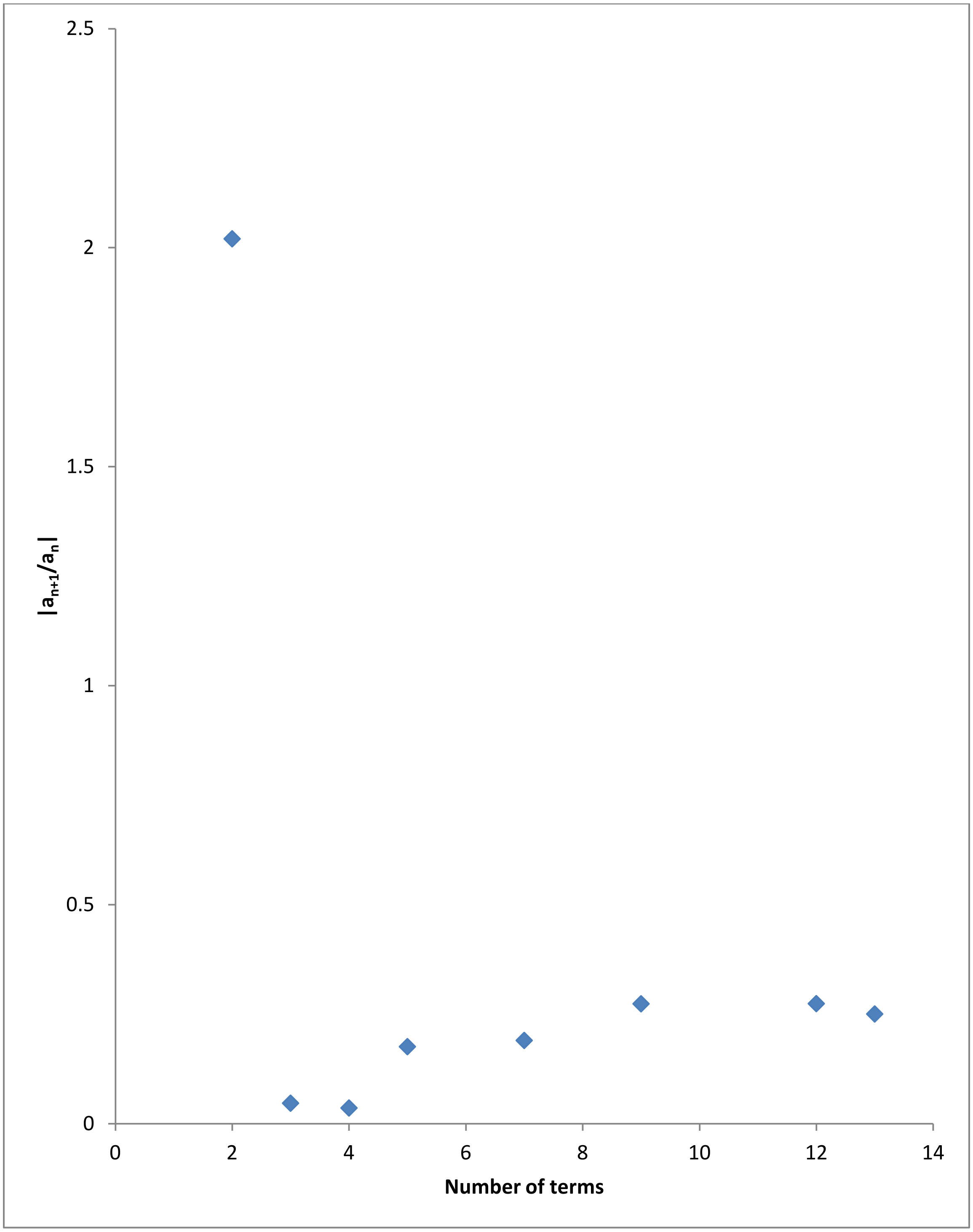


Figure 7.3. The ratio convergence test applied to the series coefficients (MDE) for ADM and HPM as a function of the number of terms in series.

ADM and HPM provide analytical solution in terms of an infinite power series (see Eqs. (7.25 – 7.27) for ADM and Eqs. (7.42 – 7.44) for HPM). The series consists of both positive and negative terms, although not in a regular alternating fashion. The ratio test was applied to the absolute values of the series coefficient. This provides a sufficient condition for convergence of the series for a space interval ΔX in the form

$$\lim_{m \to \infty} \left| \frac{a_{m+1}}{a_m} \right| < \frac{1}{\Delta X} \tag{7.78}$$

However, the approach in this study was to replace Eq. (7.78) with

$$\lim_{m \to M} \left| \frac{a_{m+1}}{a_m} \right| < \frac{1}{\Delta X} \tag{7.79}$$

where M is a large constant. The behavior of the function $f(m) = |a_{m+1} / a_m|$ for increasing values of m was then observed as presented in Figures (7.1 – 7.3). It is clear from these figures that the ratio f(m) decays as m increases, obviously indicating that the series is convergent.

Figures (7.4 – 7.7) show four snapshots in time of the tumour cell density, ECM density and MDE concentration. The ECM profile shows clearly the degradation by the MDEs. As the MDEs degrade the ECM, the tumour cells invade via combination of diffusion and haptotaxis.

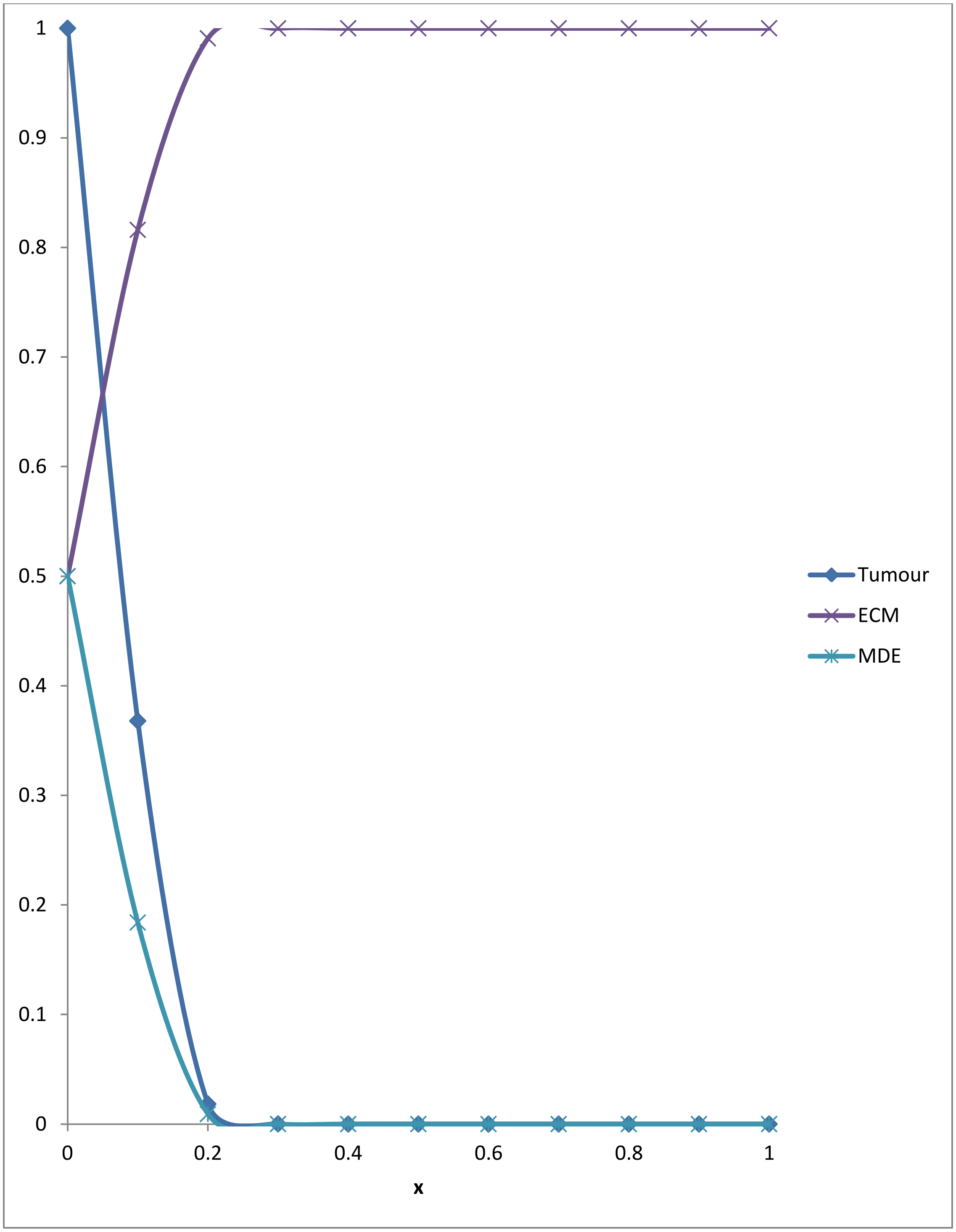


Figure 7.4. One dimensional ADM and HPM solution of the system (7.6 – 7.8) with constant tumour cell diffusion showing the cell density, MDE concentration and ECM density at t = 0.

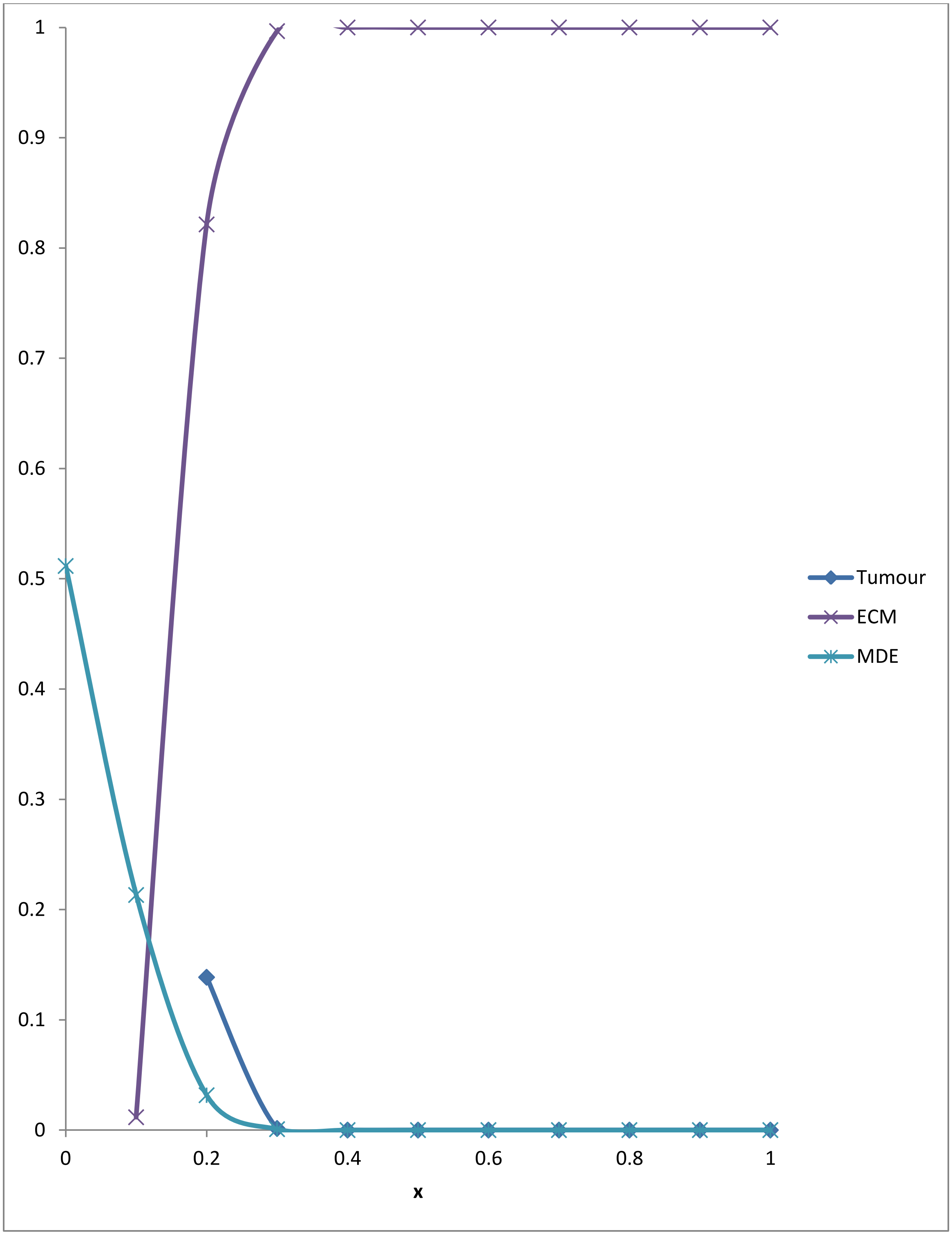


Figure 7.5. One dimensional ADM and HPM solution of the system (7.6 – 7.8) with constant tumour cell diffusion showing the cell density, MDE concentration and ECM density at t = 1.

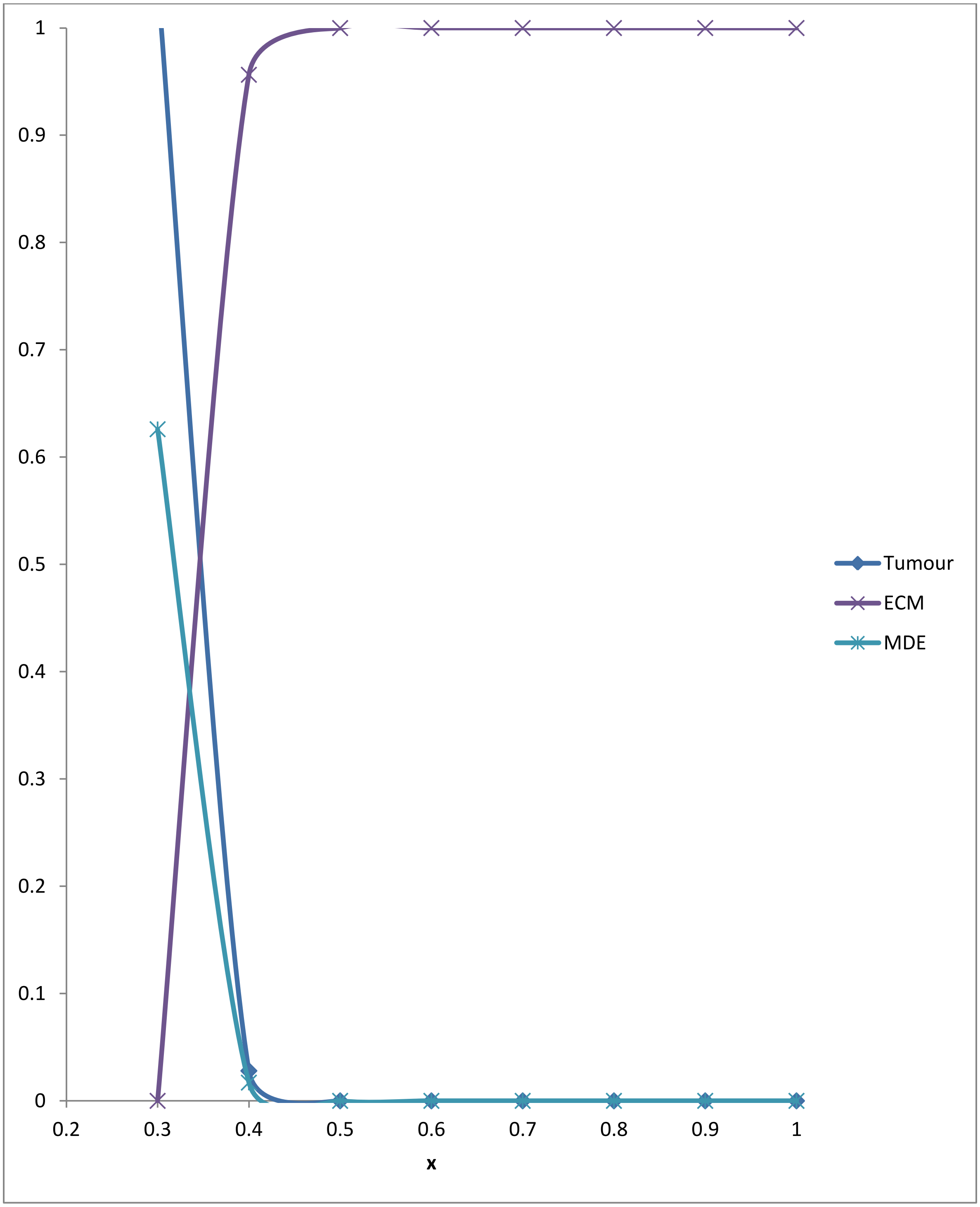


Figure 7.6. One dimensional ADM and HPM solution of the system (7.6 – 7.8) with constant tumour cell diffusion showing the cell density, MDE concentration and ECM density at t = 10.

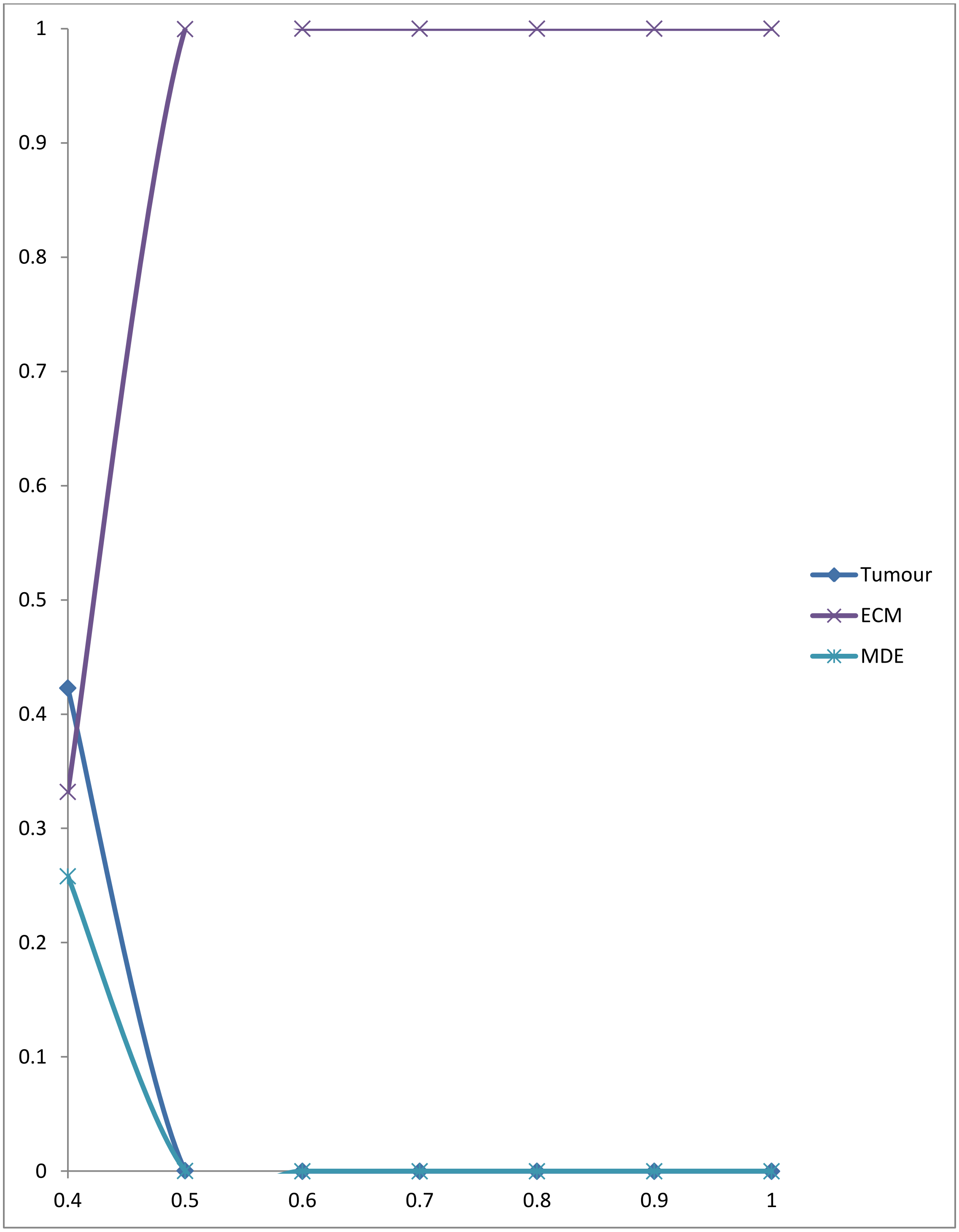


Figure 7.7. One dimensional ADM and HPM solution of the system (7.6 – 7.8) with constant tumour cell diffusion showing the cell density, MDE concentration and ECM density at t = 20.

7.7 Summary

In this chapter, we have modeled in a simple but effective manner using ADM and HPM. The solutions obtained are in convergent series form with easily computable terms. Comparison with the decomposition method shows that the homotopy perturbation method is a promising tool for finding approximate analytical solutions to strongly nonlinear problems since HPM does not involve the Adomian polynomials. Our results are in a good agreement with other models which being numerically solved.