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A Study of the Effect of Magnetic Field on the Transport of Cargos through Nuclear Pore Complex

Parul Saxena, Lokendra Kumar

Abstract- Nuclear pore complex is the largest type of macromolecular complex in the cell. In spite of their large size and complex structure NPC undergo complete breakdown and reformation at cell division. NPCs allow the transport of water soluble molecules across the nuclear envelope and can actively conduct 1000 translocations per complex per second. Small particles are able to pass through the nuclear pore complex by passive diffusion but larger particles are also able to pass through the large diameter of the pore but atmost negligible rates. Over the past few years there has been an increasing interest in the pore complex. The current challenge is to understand the effect of magnetic field and permeability on the transport of cargos from NPC using Mathematical model. For this purpose we have used bvp4c tool in Matlab. It is observed that magnetic field enhances the transport of cargos through NPC, which can be used in the cell based diseases.

Keywords-Nuclear Pore Complex, Magnetic field. Mathematics Subject Classification: 76Zxx

I. INTRODUCTION

Nuclear pore complex is one of the largest types of macromolecular complex in the cell. It has an estimated molecular mass of 15 MDa in vertebrates (Reichelt et al. [14]) comprises 50-100 proteins (Fontoura et al. [5]) termed Nucleoporins. Molecules destined for nuclear import or export can be thought of as cargos and include proteins, various types of RNA and RNPs [Fig. 1]. For recent reviews see Nakielny and Deryfuss [12], Gorlich and Kutay [7]. Allen et al. [1] have studied the nuclear pore complex as a mediator of translocation between nucleus and cytoplasm. They explained the interactions between the structural elements of the pore complex and the mechanism they derive the physical processes of translocation through it. Pores with complex have been described in this study. Mattaj and Englmeier [10] have investigated the transport of macromolecules between nucleus and cytoplasm. A large majority characterized transport involve members of the importin family of import and export receptors.Transport across the nuclear envelope (NE) occurs through the NPC, large protein aqueous structure that penetrate the NE form aqueous channels. NPCs act as permeability barrier through which specific cargos are translocated by transport receptor mediated facilitated diffusion. In principle, the translocation of export complex through asymmetrical structure NPC could be achieved unidirection movement or random diffusion have been studied by Feldherr and Akin [3], Hinshan et al. [8], Goldberg et al. [6] and Feldherr and Akin [4]. Michael and John [11] have considered NPC as a transport machine. O' Brien et al. [13] have investigated the hormonal regulation of nuclear permeability.

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* Correspondence Author (s)
Parul Saxena, Dept. of Mathematics and Astronomy, Lucknow University, Lucknow, India.
Lokendra Kumar, Dept. of Mathematics, Jaypee Institute of Information Technology, Noida, India.

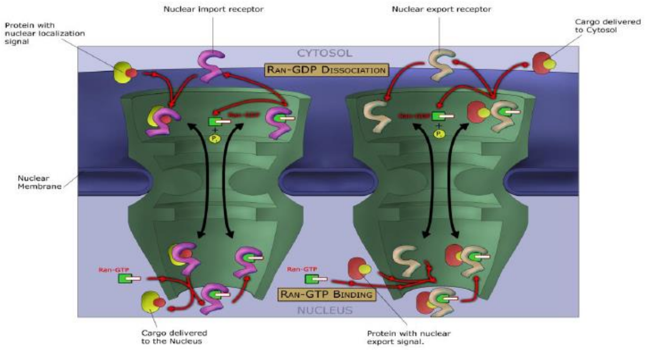

Fig. 1 RanGTP Cycle.

They investigated that short term regulation of nuclear permeability may provide a novel mechanism by which such harmones permit transcriptions factors and other regulatory molecules to enter the nucleus and thereby regulating gene transcription in target cells.Izaurraide and Mattaj [9] have investigated the transport of RNA between nucleus and cytoplasm. Studies of the import of RNA from the cytoplasm have revealed that different classes of different nuclear localization signals exist and protein components of viral RNPs that appear to determine the direction in which they move through the nuclear envelope have been identified. Becskei and Mattaj [2] have investigated the strategy for coupling the RanGTP gradient to nuclear protein export. Now in this problem our interest is to study the effect of magnetic field on the facilitated export of Cargos through NPC. For this purpose we have modified the Mathematical model proposed by Becskei and Mattaj [2] considering the effect of magnetic parameter and permeability parameter. To solve the boundary value problem we have used bvp4c tool in Matlab.This tool is used for solving linear and nonlinear boundary value problems. We converted the differential equations into first order differential equations and then apply bvp4c.

II. FORMULATION OF THE PROBLEM

To study the effect of permeability of nuclear pore complex on the movement of molecules, we have considered it as dense porous medium in which molecules diffuse very fast, Brinkman equation of motion have been used to modify the Mathematical model proposed by Becskei and Mattaj [2]. Hence in the steady state the equation of motion within the nuclear pore complex is

$$\frac{d^2n}{dx^2}-\left(\frac{K_{ON}r}{D_{NPC}}+\sigma^2\right)n=0, \qquad (1)$$

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where K_{0N} is the second order rate constant, D_{NPC} is the diffusion constant to export cargoes within the NPC and σ is the Darcy number. Eq. (1) is modified to study the effect of magnetic field (Srivastava and Saxena [16]);

$$\frac{d^2n}{dx^2}-\left(\frac{K_{ON}\,r}{D_{NPC}}+\sigma^2+M^2\right)n=0\,, \tag{2}$$

where M is the magnetic parameter. The Boundary conditions of the problem are

$$\frac{dn}{dx}=-P_N(n_c-n) \qquad at \;\; x=0, \tag{3}$$

$$\frac{dn}{dx}=0 \qquad at \;\; x=1, \tag{4}$$

Where n_c is the cytoplasmic concentration of NES cargoes, P_N is the proportionality constant and is characteristic of the rate of penetration of a free cargo into the NPC.

III. METHOD OF SOLUTION

The equation (2) with the boundary conditions (3) and (4) is reduced to a system of first –order differential equations and solved using a MATLAB boundary value problem solver **bvp4c.** This program solves boundary value problems for ordinary differential equations of the form y′ = f (x, y, **p**), a ≤ x ≤ b, by implementing a collocation method subject to general two point boundary value problem g (y(a), y(b), **p**) = 0, here **p** is a vector of unknown parameters. Boundary value problems (BVPs) arise in most diverse forms. Just about any BVP can be formulated for solution with **bvp4c**.The first step is to write the ODEs as a system of first order ordinary differential equations. The details of the solution method are presented in Shampine and Kierzenka [15] and references therein.Numerical results are obtained by taking different range of permeabilties.The results show influence of magnetic parameter on facilitated export. Export gradient has been changed with the concentrations inside the NPC, to study the effect on the motion of cargoes through NPC.

IV. RESULTS

We solve equation (2) with the boundary conditions (3) and (4) using **bvp4c.** The Numerical results are obtained for export of cargoes with different parameters and shown in Figs.2 to 6. Fig 2(a) presents the effect of permeability on the export of cargoes when dn/dx = 3.05 at x = 0.

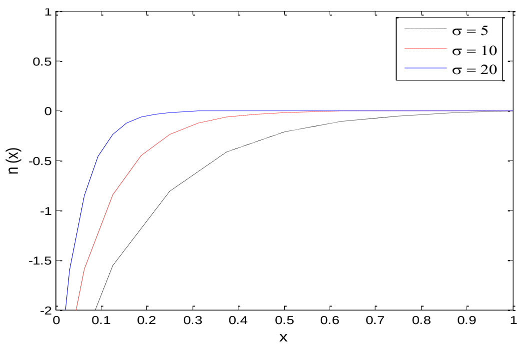

Fig. 2(a)

It is observed that with the increase of porous parameter the export of cargoes decreases. It can be seen from Fig.2 (a) that at σ = 5.0, $n(x)$ increases continuously from 0 to 1, through the whole NPC. But at σ = 10.0, it increases from 0 to 0.6 and then show constant behavior and for σ = 20.0, it achieves constant value by 0.3. As we know that this dimensionless number has reciprocal relation with permeability, the effect of permeability is to increase the export of cargoes through the nuclear pore complex. This effect has been observed in absence of Magnetic field i.e. with M = 0.Now we make the export gradient almost doudle from previous one i.e. dn/dx = 6.04, and study the effect of porous parameter on the export of cargoes.The effect of permeability on the motion of cargoes is observed to be same as in initial approach but due to increase in export gradient, transport increases in the forward direction which seems positive.

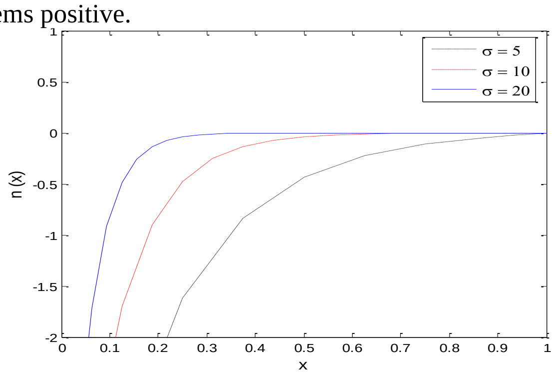

Fig. 2(b)

This is presented in Fig. 2(b). This figure can be compared from the previous figure.The analysis is very clear now that the effect of export gradient is significant on the export of cargoes as it depends on the proportionality constant and cytoplasmic concentration. On continuing the approach we have investigating the effect of export gradient by taking other two values, which are shown in Fig. 2(c) and Fig. 2(d) with dn/dx = 9.12 and dn/dx = 12.04 respectively. These Figures show the change in export process with permeability as well as the export gradient. We observe the same behavior of export with permeability in these figures i.e. it increases with the permeability of the pores of nuclear pore complex but there is change with the increase of export gradient.

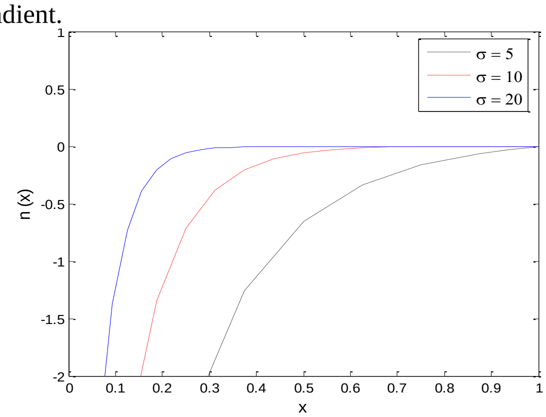

Fig. 2(c)

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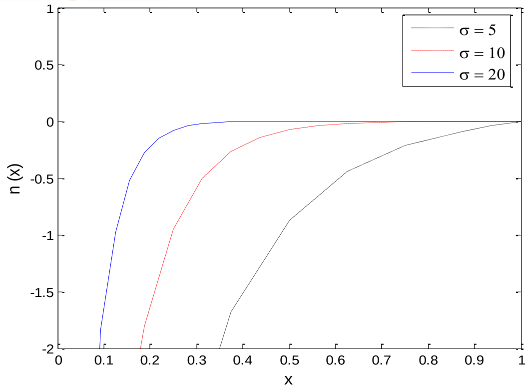

Fig. 2(d)

Now we are going to discuss another important factor which affects the export process significantly i.e. the concentration effect of RanGTP. The export of cargoes is investigated for dn/dx = 3.05 at x = 0 and σ = 5.0, 10.0, 20.0, when the RanGTP concentration is small. This effect can be observed in Fig.3(a).For this case export of cargoes again increases with permeability. For all three values export starts between x = 0 and x = 0.1. It is investigated the on the export of cargoes the effect of export gradient and the effect of low concentration is almost same. Now we increase the concentration slightly let

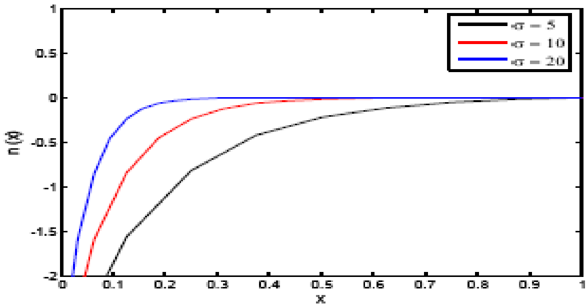

Fig.3(a)

R = 10.05, where $R = K_{0N}r/D_{NPC}$. The export phenomena in this case can be observed from Fig.3(b). From this figure it can be seen that export of cargoes at σ = 5.0 comes closer to σ = 10.0 that means concentration tends to reduce the effect of porous parameter. For further study we take just triple value of the value taken in Fig. 3(b) and this is shown in Fig 3(c). The same effect on export is observed but at extremely high value of concentration the effect of porous parameter is negligible. This is the reason that small particles are able to pass through the nuclear pore complex by

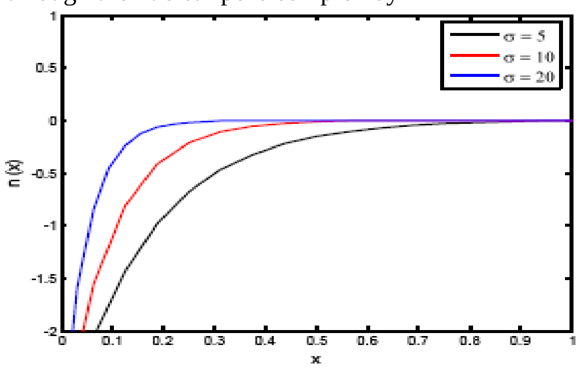

Fig.3(b)

passive diffusion while larger particles only pass through the large diameter of the pore but at almost negligible rates. This behavior is shown in Fig. 3(d).

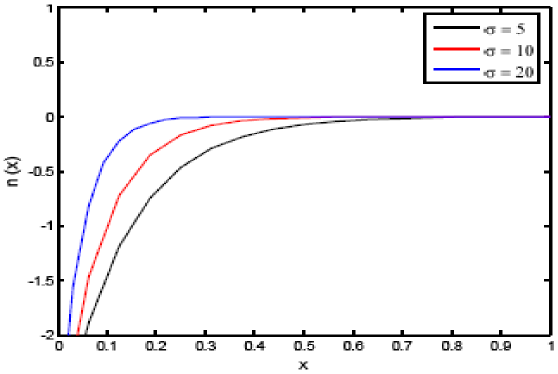

Fig. 3(c)

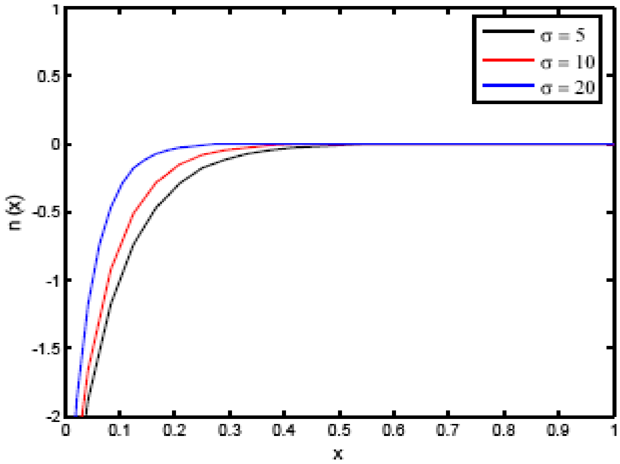

Fig. 3(d)

Now we are going to discuss the effect of magnetic field on the export of cargoes. For this purpose we have taken the value of export gradient dn/dx = 7.45, at x = 0 and M= 2.0, 4.0, 6.0. For σ = 5.0, the behavior can be viewed in Fig. 4(a), magnetic field enhances the export of cargoes through the nuclear pore complex. It is observed for σ = 10.0 the effect of magnetic field on the export of cargos seems slow. (Fig. 4 (b)). The effect of magnetic field in both figures on the export of cargoes is different just because of change in porous parameter. Indirectly it shows that if permeability of pores inside the nuclea pore complex decreases the effect of magnetic field also decreases and export profiles becomes closer. For clear view of this analysis we have considered two more values of porous parameter, since the permeabilities of pores inside the nuclear pore complex are small. We consider the high values of porous parameter.

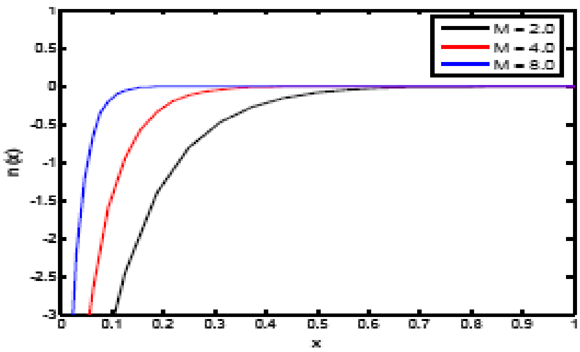

Fig.4(a)

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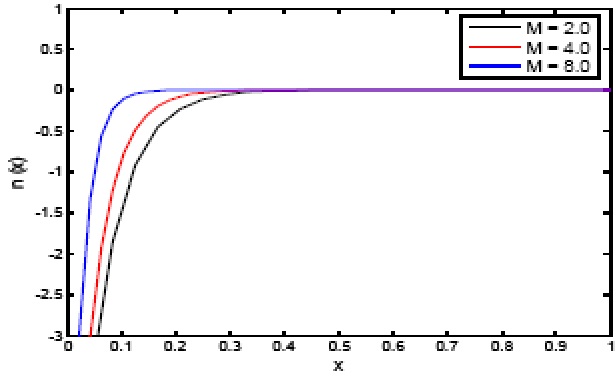

Fig. 4(b)

Fig. 4(c) and Fig.4 (d) can be viewed which are plotted for σ = 20.0 and σ = 25.0. These figures clearly show that porous parameter tends to reduce the effect of magnetic field.These results may be very useful in magnetic devices, which are formed for curing typical diseases in human.

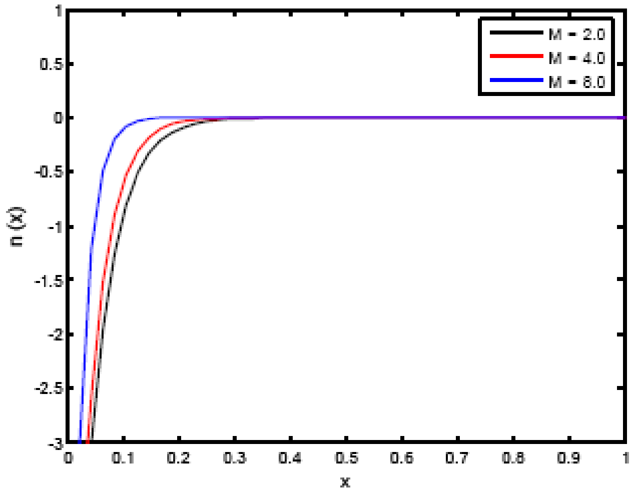

Fig. 4(c)

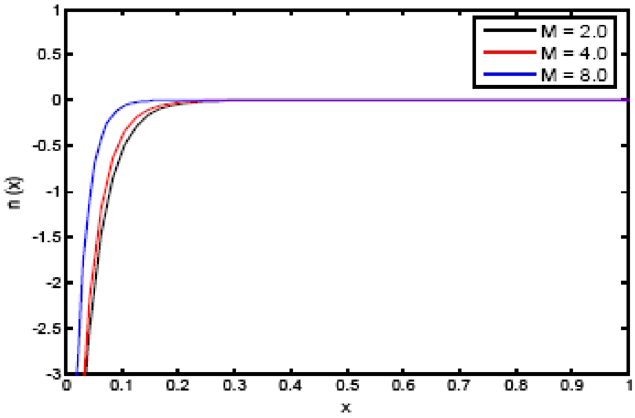

Fig. 4(d)

Concentration of RanGTP affects the motion of cargoes, under the effect of magnetic field. To study the change in movement of cargoes for particular export gradient has been investigated with magnetic field simultaneously with concentration. Firstly we take, R = 10.29, M = 2.0, 4.0, 6.0, dn/dx = 7.45 at x = 0 and σ = 10.0 and this change is presented in Fig. 5 (a). From this Figure it can

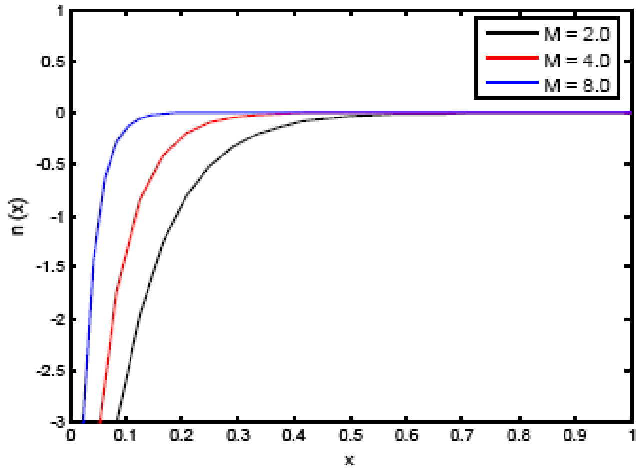

Fig. 5 (a)

be seen that the effect of magnetic field is to increase the export of cargoes through the nuclear pore complex. But as there is slight increase in the concentration the influence of magnetic field on the export process tends to decrease, which is shown in Fig. 5 (b). For Further study of concentration effect, we take *R* = 201.32, The effect can be viewed in Fig. 5(c). To study the effect of high concentration of RanGTP, we take *R* = 500.0 and it is observed that the effect of magnetic field on the motion of cargoes is almost negligible and there is need of high magnetic field intensity. The export of cargoes for this case is presented in Fig. 5(d). For clarifying the concentration effect with magnetic field the figures are shown below.

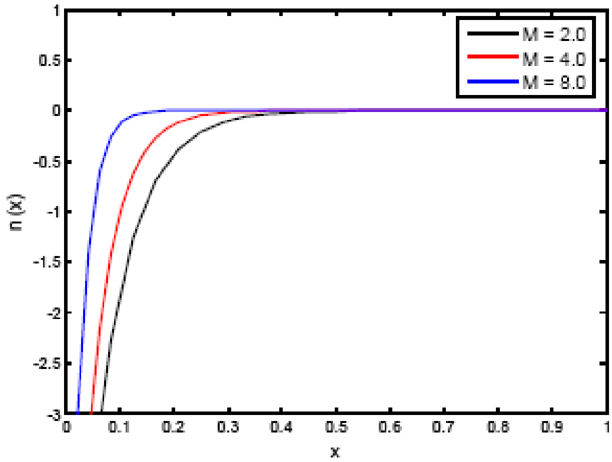

Fig. 5(b)

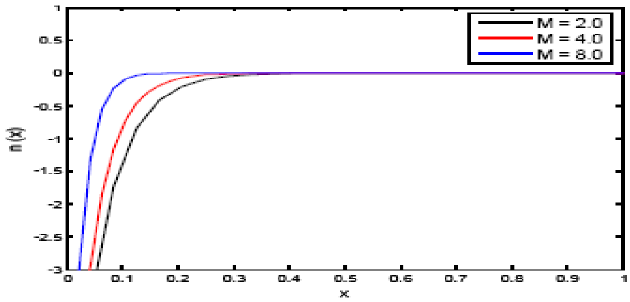

Fig. 5(c)

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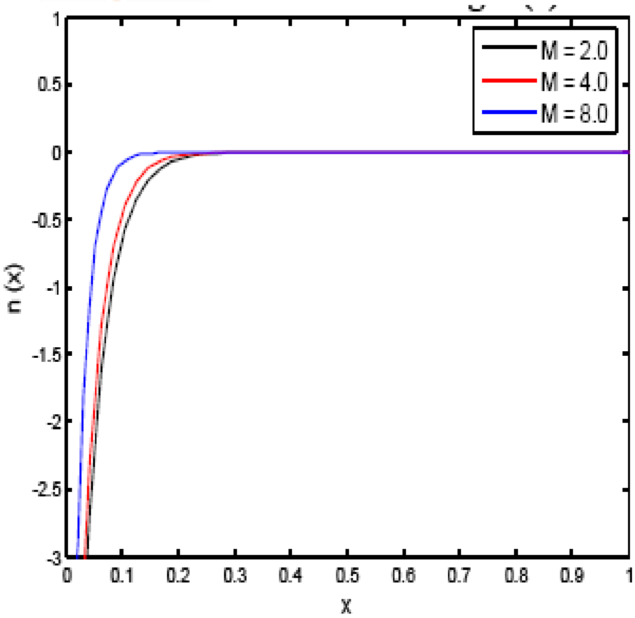

Fig. 5(d)

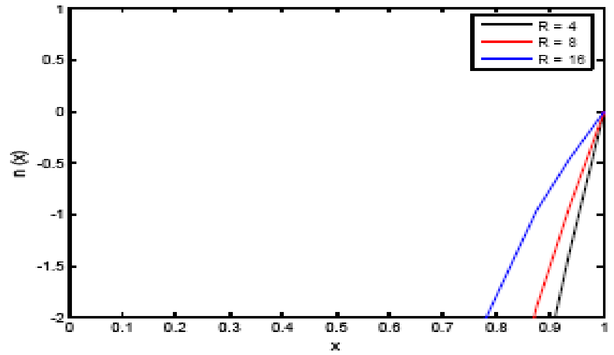

Fig. 6 (a)

Now we are going to discuss the simultaneous effect of porous parameter and magnetic field, with small concentrations. Taking R = 4.0, 8.0, 16.0, M= 2.0 and σ = 2.0, the effect on export of cargoes can be seen in Fig.6(a). To discuss the effect of magnetic field and porous parameter simultaneously we have run this program for different values of M and σ.

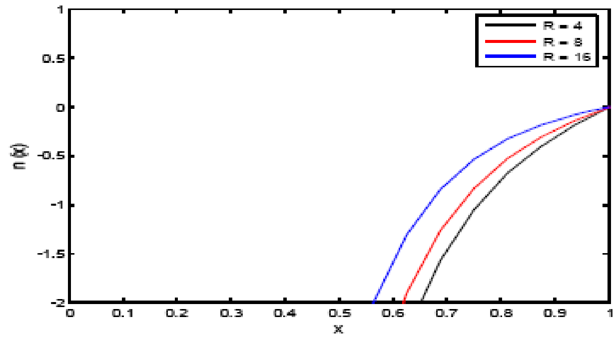

Fig. 6(b)

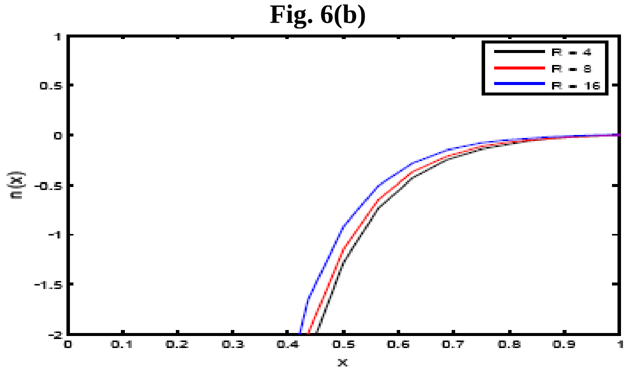

Fig. 6(c)

The behavior can be seen in Fig. 6(b) for M = 4.0 and σ = 4.0.Fig. 6 (c) has been plotted by taking M = 8.0 and σ = 8.0.It is observed that as we increase the magnetic field and porous parameter simultaneously the effect of RanGTP on the export of cargoes becomes less. Fig. 6(d) is plotted with high values of porous parameter and magnetic field. It can be seen from the figure that the effect of increase of concentration on the movement of cargoes is almost negligible.

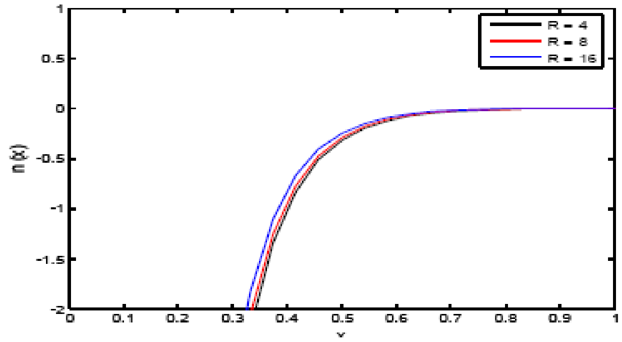

Fig. 6 (d)

CONCLUSIONS

The work investigated the effect of applied magnetic field and the permeability on the facilitated export of cargoes form nuclear pore complex. The governing equations are approximated to a system of ordinary differential equations. Numerical calculations are carried out for various values of the dimensionless parameters of the problem using an efficient and easy to use MATLAB routine **bvp4c**.The results are presented graphically and we conclude that the flow and quantities of physical interest are significantly influenced by these parameters. The effect of increase the perm abilities of pores within the nuclear pore complex increases the export of cargoes. Since there is numerous nuclear pore complexes within nuclear envelope the nature of pores inside it differ, which affects the export process significantly.The effect of concentration of RanGTP have been explained using the model described above and it is predicted, that the region having small concentration of Ran GTP within nuclear pore complex, affected by applied magnetic field more significantly in comparision of the regions of high concentration.

In addition the present analysis has shown that the effect of increasing perm abilities of pores within the nuclear pore complex enhances the export of cargoes through the nuclear pore complex. This analysis can be useful for further study of cell division, cell growth and DNA damage and repair. Since the effect of Magnetic field has been shown with variation of different physical entities therefore this concept can be implemented in the cure of cell based diseases like cancer.

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