Effect of Gradient Magnetic Fields on Molecular Diffusion Through Cell Membranes: A Theoretical and Numerical Study

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Abstract: The diffusion of biologically active molecules is a fundamental and ubiquitous process that governs numerous mechanisms and defines the characteristic time scales of essential cellular activities. In this work, we investigate how a strong static magnetic field (MF) influences the diffusion behaviour of both paramagnetic and diamagnetic species within a human cell. We first describe the influence of a homogeneous static magnetic field on molecular diffusion, and subsequently, for the first time, derive an analytical expression that includes the effects of a non-uniform magnetic field. Both equations were solved numerically, revealing that the influence of magnetic field non-uniformity becomes significant only in the presence of high gradinet magnetic fields. In contrast, for weak gradient magnetic fields, their effect on the diffusion of biologically active molecules is smaller, yet it cannot be neglected compared to a homogeneous field.

Keywords: electromagnetic field, molecular diffusion, diffusion equatin.

1. Introduction

In recent years, there has been growing interest in the effects of electromagnetic fields on biological systems. Research has focused on the potential relationship between these fields and certain types of cancer, as well as their cytotoxic and genotoxic properties. The effects of magnetic fields on diffusion have been studied since the earliest observations involving the influence of both static uniform and non-uniform magnetic fields on the diffusion of paramagnetic species [1,2]. Interactions between magnetic fields and living cells can give rise to a range of biomagnetic effects at both the cellular and organismal levels [3–6]. Reference [7] highlights recent advances in elucidating the fundamental mechanisms through which magnetic gradient forces influence cell fate specification and differentiation. It is shown here that the concentration-gradient magnetic force can drive the diffusion of both paramagnetic and diamagnetic species within cells.

Our work provides a novel contribution by specifically analyzing the influence of non-uniform magnetic fields on the diffusion of biologically active molecules across the

cell membrane, which represents a slight extension of the very interesting research presented in [8]. Although the concentration-gradient magnetic forces acting on diffusing molecules are relatively small, we show that the effect of the magnetic field gradient can be significant in the presence of sufficiently strong gradient magnetic fields.

2. Results and Discussion

When a static magnetic field is applied to cell systems, three types of magnetic forces can act on subcellular components, molecules, and ions [7]: (i) the Lorentz force, $\boldsymbol{F}_L = q(\boldsymbol{v} \times \boldsymbol{B})$ (where $\boldsymbol{B}$ is the magnetic induction, q is the ion electric charge, and $\boldsymbol{v}$ is its velocity); (ii) the magnetic gradient force, $F_{\nabla B} \propto \nabla B^2$ (when the magnetic field is uniform ($\nabla B = 0$), the magnetic gradient force is zero); (iii) the concentration-gradient magnetic force, $F_{\nabla n} \propto B^2 \nabla$n (where ∇n is the gradient of the concentration of diamagnetic and paramagnetic species, and ∇ is the differential operator nabla).

The concentration-gradient magnetic force will be considered as the driving force describing the static homogeneous MF's effect on diffusion in cells. In fact, living cells are far from having a thermodynamic equilibrium, and hundreds of diamagnetic and paramagnetic species inside cells may have very large concentration gradients. In this case, the magnetic concentration-gradient force acts on diamagnetic and paramagnetic molecules and can either assist or oppose ion movement through the cell.The volume density of the concentration-gradient magnetic force per molecule is given by $\boldsymbol{f}_1 = \frac{\chi B^2}{2\mu_0 n N_A} \nabla n$. Under this force, the flow velocity u of a paramagnetic or diamagnetic solute is given by $u = \gamma f_1$, where γ is the mobility of the diffusing molecule in solution. Depending on the sign of the magnetic susceptibility ($\chi < 0$ for diamagnetic and $\chi > 0$ for paramagnetic species), the force acts either parallel or antiparallel to the concentration gradient. The differential equation that describes the diffusion of molecules in a solution moving with velocity u, in the diffusion approximation, is described as

$$\frac{\partial n}{\partial t} = D\nabla^2 n - (\nabla \cdot n\boldsymbol{u}) = D_{eff}\nabla^2 n \quad (1)$$

where D is the diffusion coefficient, and $D_{eff} = \left(D - \frac{\gamma \chi B^2}{2\mu_0 N_A}\right)$ is the effective diffusion coefficient. Given that the mobility (γ) of the diffusing molecule in a solution may be calculated using the Nernst–Einstein relation,$\gamma = D/k_B T$ (where k_B is the Boltzmann constant and T is the temperature), one can arrive at: $D_{eff}(B) = D(1 - \beta)$, where $\beta = \frac{\chi B^2}{2\mu_0 RT}$ and R=8.31 J/(K mol) is the gas constant.

In the case when a nonuniform static magnetic field ($\nabla B \neq 0$) is applied to a cell, the force acting on the molecules now also includes the magnetic gradient force. Thus, the differential equation describing the diffusion of molecules in this case is modified to account for the additional effects of the magnetic gradient force. The volume density of the concentration-gradient magnetic force plus the magnetic gradient force is given by

$$n\boldsymbol{u} = n\gamma \boldsymbol{f} = n\gamma(\boldsymbol{f}_{1\nabla n} + \boldsymbol{f}_{2\nabla B}) = n\gamma\left(\frac{\chi B^2}{2\mu_0 n N_A}\nabla n + \frac{n\chi B}{\mu_0 n N_A}\nabla B\right). \quad (2)$$

After a few algebraic transformations, after linearization and retaining first-order inhomogeneities ∇B, in the non-uniform field, the diffusion equation (1) becomes:

$$\frac{\partial n}{\partial t} = D(1-\beta)\nabla^2 n - 4D\beta\frac{\nabla B}{B}\nabla n. \quad (3)$$

In spherical symmetry, equations (1) and (3) become:

$$\frac{\partial n}{\partial t} = D(1-\beta)\left(\frac{\partial^2 n}{\partial t^2} + \frac{2}{r}\frac{\partial n}{\partial r}\right), \quad (4)$$

$$\frac{\partial n}{\partial t} = D(1-\beta)\left(\frac{\partial^2 n}{\partial t^2} + \frac{2}{r}\frac{\partial n}{\partial r}\right) - 4D\beta\frac{\nabla B}{B}\frac{\partial n}{\partial r}. \quad (5)$$

We solved equations (4) and (5) using basic boundary and initial conditions for simplicity: $n(t,0)=0, n(t,R)=n_0,$ and $n(0,r)=g(r)$ where n_0 is the constant concentration at the surface of the sphere, $r=R$, and the function $g(r)$ is the initial concentration inside the sphere. We used the central difference approximation of the derivative of n at the (i,j)-th node

$$n_{i,j+1} = n_{i-1,j}\left[c-\left(\frac{g}{r}-f\right)\right] + n_{i,j}[1-2c] + n_{i+1,j}\left[c+\left(\frac{g}{r}-f\right)\right] \quad (6)$$

where $c=\frac{D(1-\beta)\Delta t}{(\Delta r)^2}$, $g=\frac{D(1-\beta)}{\Delta r}$ and $f=\frac{4D\beta\frac{\nabla B}{B}}{2\Delta r}$. To prevent the problem of singularity at grid points $r=0$, we used the approximation $\lim_{r\to 0}\left(\frac{2}{r}\frac{\partial n}{\partial r}\right)=\left(2\frac{\partial^2 r}{\partial r^2}\right)_{r=0}$. We plot of $N(r,t)/N_0$ for: 1) Weak Gradient Magnetic Field (WGMF) - in commercially available worldwide MRI scanners $B\sim 2T$, the gradient magnetic field is $\frac{\nabla B}{B}\sim 50\text{mT/m}$. For this case solve the diffusion equation (4) (uniform static magnetic field) and diffusion equation (5) (nonuniform magnetic field) respectively, if: $\beta\sim 0.5$ (paramagnetic species in MF), $\beta\sim -0.5$ (diamagnetic species in MF), and $\beta=0$ (no magnetic field); 2) High Gradient Magnetic Field (HGMF) - $B\sim 71.76\text{T}$ and $\nabla B=10^6\text{T/m}$ if $\beta\sim 0.5$, $\beta\sim -0.5$, and $\beta=0$ respectively (see Fugure 1).

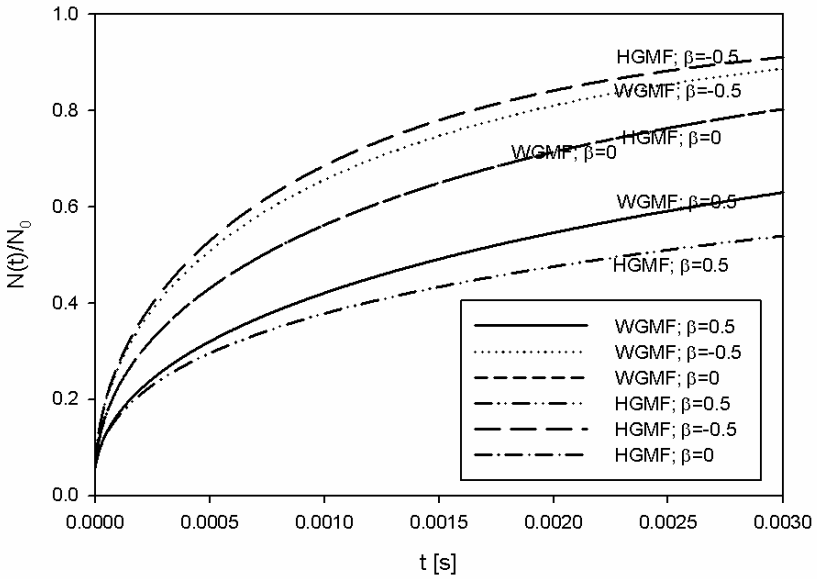

Figure 1. Magnetic Fields effect on diffusion in sphere: WGMF - Weak Gradient Magnetic Field, HGMF- High Gradient Magnetic Field.

In Figure 1, we show the solution for Equation (5) as the plots of $N(r,t)/N_0$, the total amount of diffusing substance entering the sphere for the three cases: diffusion with no magnetic field ($\beta=0$) and diffusion in a magnetic field ($\beta=0.5$ and $\beta=-0.5$). The calculations of $N(r,t)/N_0$were

performed for $R = 5\mu m$, $D = 10^{-9} m^2/s$ which is the O_2 diffusivity inside a red blood cell (RBC) [8].

Thus, the diffusion process influenced by the concentration-gradient magnetic force is described by Equations (4,5) with $D_{eff}(B) = D(1 - \beta)$, which constitutes a partial differential equation. It is easily shown that, a magnetic field decreases ($\beta > 0$) the diffusion coefficient for paramagnetic molecules and increases it ($\beta < 0$) for diamagnetic molecules. By numerically solving our Equation (5) for the concentration-gradient magnetic force in the case of a magnetic field gradient, we confirmed the assumption that a gradient field, as a small perturbation, additionally influences the rate of the diffusion process, particularly in the case of a strong magnetic field gradient (Figure 2).

3. Conclusions

This study examines the impact of a strong static magnetic field (MF) on the diffusion dynamics of paramagnetic and diamagnetic species inside a human cell. We first address the role of a uniform static MF in molecular diffusion, and then, for the first time, present an analytical formulation that incorporates the effects of a spatially varying magnetic field. Numerical solutions of both formulations demonstrate that magnetic field non-uniformity has a pronounced influence only under conditions of high magnetic field gradients. For weak gradients, the effect on the diffusion of biologically active molecules is less pronounced, yet remains non-negligible when compared to the case of a homogeneous field..

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