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A MICROFLUIDIC MODEL FOR THE MIGRATION OF CHONDROCYTE UNDER PULSED ELECTROMAGNETIC FIELD

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ABSTRACT

Pulsed electromagnetic field (PEMF) treatment is a potentially non-invasive method for tissue engineering. In this paper, a theoretical model is established to simulate the regeneration of articular cartilage for Osteoarthritis by means of pulsed electromagnetic fields (PEMF). The electrical field, flow field, single particle motion and concentration field during the growth of chondrocyte are obtained by solving the theoretical model numerically, which accounts for cell distribution in the culture dish. The induced electric field strength can be numerically obtained by Maxwell's equation and then the potential distribution by the Poisson equation and Laplace equation. The chondrocytes can be driven to move once the electric field is built up. In the calculation of the flow field, the continuity and momentum equation are applied to obtain the bulk electroosmotic velocity field which will affect the motion of the charged cell due to viscous drag forces. The motion of a single particle can be obtained by the classic Newton's second law. In addition to a single particle, the concentration distribution of particles which indicates the migration of chondrocytes can be described by the conservation law of mass. Boundary conditions are required to solve these sets of equations numerically. A comparison between model results and actual experimental data for the growth and migration of chondrocytes is performed. The results presented here allow a better understanding of the role PEMF in the treatment of Osteoarthritis.

INTRODUCTION

The issue of Osteoarthritis treatment is an extremely urgent health and socio-economic problem. In Osteoarthritis, the cartilage in joints has become damaged, disrupting the smooth gliding motion of the joint surfaces. It is often described as "wear and tear" arthritis, causing swelling, pain and disability of the person [1]. It is estimated that about 85% of Canadians by the age of 70 will be affected by Osteoarthritis, which has caused an economic impact of over $65 billion dollars according to the Arthritis Foundation [2].

Up to date, many approaches have to employed to stimulate the regeneration of articular cartilage, which is the key factor for the treatment, but not one method is both effective and painless, either drugs or surgeries [3, 4]. The ideal method for treating Osteoarthritis would require effective repair of cartilage defects using a device that operates in a non-invasive manner.

Since the approval by US Food and Drug Administration (FDA) in 1979, pulsed electromagnetic field (PEMF) has been widely used to treat non-union fractures and other related problems in bone healing [5, 6]. In PEMF treatment, Electromagnetic field can be delivered to biological system by using direct placement of an electrode or non-invasively by capacitive coupling (opposing electrodes placed on skin across the target area) or inductive coupling (PEMF induce an electric current in the target area without skin contact altogether). Moreover, little risk has been found to be associated with PEMF therapy after many years of global usage [7, 8]. Similar reasons can be employed to justify the use of PEMF treatment for diseases involving cartilage. However, the lack of a fundamental understanding and convincing scientific evidence has been delaying the use of PEMF in treating Osteoarthritis for any future clinical study.

In our work, a simultaneous experiment and simulation are conducted to investigate the effect of PEMF on chondrocytes. Two Helmholtz coils are employed in the experiment *in vitro* to generate an uniform induced electric field which is the key factor for the growth and migration of chondrocytes. Articular cartilage consists of an extra-cellular matrix of chondrocytes with large proteoglycan molecules whose glycosaminoglycan side chains are negatively charged [9]. The fluid surrounding these molecules contains many positively charged counter-ions that balance those of the negatively charged side chains. When the cartilage is loaded with fluid, the positively charged ions are

displaced and an electric field is produced by the separation of charges. These electric fields are termed as streaming potentials. It is commonly thought that analogous to the response in bone, the production of these streaming potentials is in part responsible for the migration and proliferation of chondrocytes [10]. In this paper, the electrical field, flow field, single particle motion and concentration field during the growth of chondrocyte are obtained by solving the theoretical model numerically, which accounts for cell distribution in the culture dish.

NOMENCLATURE

$\mathbf{\Psi}$	the total electric potential
ϕ	the externally applied potential
ψ	the surface potential of charged cells
V_m	the amplitude of sawtooth wave
T	the period of sawtooth wave
R_{coil}	the resistance of the winding coil
$\mathbf{B}$	the magnetic field of two Helmholtz coils
μ_0	the permeability of free space
N	the number of windings
H	the height of coil
$\mathbf{E}$	the induced electric field by $\mathbf{B}$
ρ_e	the net charge density
ε	the dimensionless dielectric constant of the solution
ε_0	the permittivity of vacuum
k_b	the Boltzmann's constant
e	the fundamental charge
n_∞	the ionic number concentration in the bulk solution
z	the ionic valence
T	the absolute temperature
κ^{-1}	the Debye length defined as the thickness of EDL
r_s	the radius of the cell
ψ_s	the surface potential at $r' = r_s$
$\mathbf{V}_{eo}$	the bulk electroosmotic velocity vector
ρ	the density of the liquid
$\mathbf{P}$	the pressure
μ	the liquid viscosity
υ	the kinematical viscosity
R_{dish}	the radius of the culture dish
$\mathbf{F}_E$	the electrostatic force
$\mathbf{F}_h$	the hydrodynamic force
m_p	the mass of the particle
$\mathbf{V}_p$	the translational velocity
$\mathbf{n}$	the normal vector pointing outward the drag force
$\mathbf{p}$	the pressure
$\boldsymbol{\tau}$	the viscous stress tensor
$\mathbf{J}$	the moment of inertia of the particle
$\mathbf{T}_p$	the torque on the particle (about the center of particle)
$\mathbf{w}_p$	the angular velocity
$\mathbf{r}$	the radius vector of the chondrocyte
C_i	the concentration of the *i*th species
D_i	the diffusion coefficient of the *i*th species
R_i	source or sink term
$\mathbf{V}_{epi}$	the electrophoretic velocity vector
μ_{epi}	the electrophoretic mobility

I. Experimental Model

Two Helmholtz coils have been employed and the setup is shown schematically in Fig 1. It can be seen that two parallel coils are spaced with one radius apart. Each coil which is 4 cm in inner radius and 1 cm in height has 120 turns of 22 AWG magnet wire. A Plexiglas stand is used to support the culture dish which contains the cell culture so that the bottom of the dish is located 2 cm from the middle of each winding coil. A second Plexiglas stand is used to superpose the symmetric axes of the tissue incubator and the coils. The placement is important to maintain the uniformity of the magnetic field which generates the induced electric field and is the key factor for the growth and migration of chondrocytes.

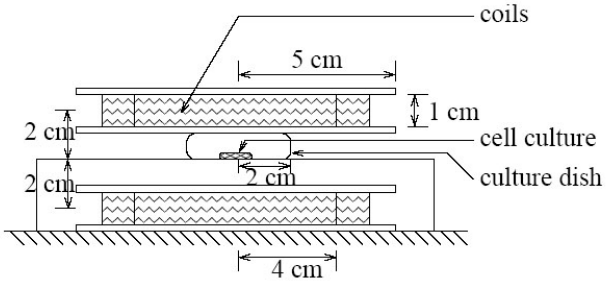

Fig 1: Schematic for a PEMF device using two Helmholtz coils

II. Theoretical Model

Until now, there is not a canonical model to describe the migration of chondrocytes under the influence of PEMF. The only model available is dated back to 1987 from Frank and Grodzinsky who mathematically modeled the stress response of cartilage cells and is not directly relevant to the chondrocyte growth and migration discussed here. The fundamental physics of chondrocyte migration is scientifically similar to those of the electric double layer (EDL) phenomena in electrokinetic microfluidics. The extra-cellular matrix of chondrocytes in articular cartilage consists of large proteoglycan molecules whose glycosaminoglycan side chains are negatively charged, while the surrounding fluid contains many positively charged counter-ions that balance the negative charge [9]. Therefore, an electrical double layer (EDL) will be formed as depicted in Fig 2. Thus, electrokinetic phenomena (e.g. Electroosmosis (EO) and Electrophoresis (EP)) will occur when an external electric field is applied. In order to understand the transport processes of the chondrocytes, theoretical models are required for the electrical field, flow field, single particle motion and concentration field.

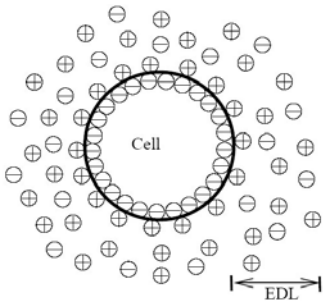

Fig 2: Schematic of the formation of an EDL near the surface of a charged cell

Electrical Field

The total electric potential Ψ is given by the superposition of the externally applied potential ϕ and the surface potential of charged cells ψ, that is,

$$\Psi = \phi + \psi \tag{1}$$

In this case, PEMF is employed to induce the electric field instead of directly applying an external electric field. Two Helmholtz coils are used and a sawtooth voltage is applied as the input signal of each coil. The expression for *v(t)* over the period *t* = 0 to *t* = *T* is

$$v(t) = \left(\frac{V_m}{T}\right)t \tag{2}$$

and the current in the winding coil is

$$i(t) = \left(\frac{V_m/R_{coil}}{T}\right)t \tag{3}$$

where V_m and T is the amplitude and period of sawtooth wave and R_{coil} is the resistance of the winding coil. Therefore, the magnetic field at the center of the coil can be written as

$$B_0(t) = \mu_0 \frac{N}{H} i(t) = \mu_0 \frac{N}{H}\left(\frac{V_m/R_{coil}}{T}\right)t \tag{4}$$

where μ_0 is the permeability of free space, *N* is the number of windings and *H* is the height of coil. Thus, the magnetic field from two Helmholtz coils arrangement can be obtained by superimposing the two constituent fields, as shown in Fig 3.

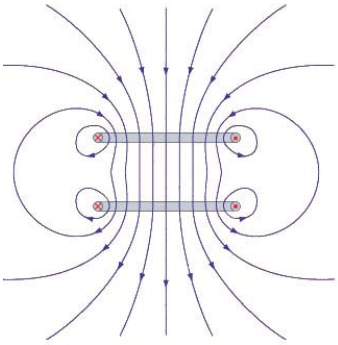

Fig 3: Schematic of the magnetic field from two Helmholtz coils arrangement

$$B(t) = 2B_0(t) = 2\mu_0 \frac{N}{H}\left(\frac{V_m/R_{coil}}{T}\right)t = mt \tag{5}$$

As $\mu_0, N, H, V_m, R_{coil}, T$ are constant, assume $\mu_0 \frac{N}{H}\left(\frac{V_m/R_{coil}}{T}\right) = m$.

According to Maxwell's Equations, the induced electric field strength can be calculated by Faraday's Law of induction

$$\nabla \times \mathbf{E} = -\frac{\partial \mathbf{B}}{\partial t} \tag{6}$$

In Cylindrical Coordinates (r, θ, z), $\mathbf{B} = mt\hat{\mathbf{z}}$ where $\hat{\mathbf{z}}$ is a unit vector along the axis of the coil and Eq. (6) can be rewritten as [11]

$$\begin{aligned} [\nabla \times \mathbf{E}]_r &= \frac{1}{r}\frac{\partial E_z}{\partial \theta} - \frac{\partial E_\theta}{\partial z} = 0 \\ [\nabla \times \mathbf{E}]_\theta &= \frac{\partial E_r}{\partial z} - \frac{\partial E_z}{\partial r} = 0 \\ [\nabla \times \mathbf{E}]_z &= \frac{1}{r}\frac{\partial}{\partial r}(rE_\theta) - \frac{\partial E_r}{\partial \theta} = m \end{aligned} \tag{7}$$

It is assumed in this case that the induced electric field is uniform in the space between the two Helmholtz coils. According to the right hand rule, the induced electric field will curl around the culture dish in concentric circles. If we consider the plane of dish parallel to the coils, as shown in Fig 4, the boundary conditions for Eq. (7) are

$$E_z = 0,\ E_r = 0 \text{ and } E_\theta(r = 0) = 0$$

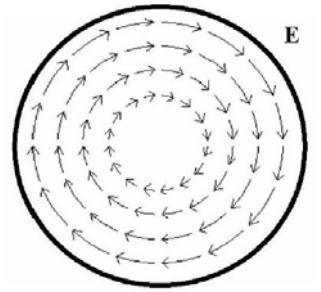

Fig 4: Schematic of the induced electric field in the plane of the culture dish generated by a steadily ramping magnetic field

Eq. (7) can be rewritten as

$$\begin{aligned} [\nabla \times \mathbf{E}]_r &= -\frac{\partial E_\theta}{\partial z} = 0 \\ [\nabla \times \mathbf{E}]_\theta &= \frac{\partial E_r}{\partial z} = 0 \\ [\nabla \times \mathbf{E}]_z &= \frac{1}{r}\frac{\partial}{\partial r}(rE_\theta) = m \end{aligned} \tag{8}$$

Solving the set of equations by the boundary conditions yields

$$E_r = 0, E_\theta = \frac{m}{2}r, E_z = 0 \tag{9}$$

Once the induced electric field strength is known, the external electrical potential can be calculated by

$$\phi(r) = -\int \mathbf{E} \cdot \mathrm{d}\mathbf{s} = -\int_0^r \frac{m}{2} r\,dr = -\frac{m}{4}r^2 \tag{10}$$

According to the theory of electrostatic, the governing equation for the surface potential ψ inside the EDL produced by the charged cell is the Poisson equation

$$\nabla^2\psi = -\frac{\rho_e}{\varepsilon\varepsilon_0} \tag{11}$$

where ρ_e is the net charge density, ε is the dimensionless dielectric constant of the solution and ε_0 is the permittivity of vacuum. The charge density ρ_e is given by the Boltzmann distribution for a symmetric electrolyte as

$$\rho_e = -2n_\infty ze\sinh(\frac{ze}{k_bT}\psi) \tag{12}$$

where k_b is the Boltzmann's constant, e is the fundamental charge, n_∞ is the ionic number concentration in the bulk solution, z is the ionic valence and T the absolute temperature (the body temperature here).

Therefore, the Poisson equation (11) can be rewritten in local Cylindrical Coordinates (r',θ',z') of the chondrocyte as the Poisson-Boltzmann equation

$$\frac{1}{r'}\frac{\partial}{\partial r'}(r'\frac{\partial\psi}{\partial r'}) + \frac{1}{r'^2}\frac{\partial^2\psi}{\partial\theta'^2} + \frac{\partial^2\psi}{\partial z'^2} = \frac{2n_\infty ze}{\varepsilon\varepsilon_0}\sinh(\frac{ze}{k_bT}\psi) \tag{13}$$

If we consider the plane of dish parallel to the coils, the following boundary conditions for Eq. (13) can be assumed:

$$\frac{\partial\psi}{\partial\theta'} = 0, \frac{\partial\psi}{\partial z'} = 0 \tag{14}$$

Thus, the Eq. (13) can be simplified as

$$\frac{1}{r'}\frac{\partial}{\partial r'}(r'\frac{\partial\psi}{\partial r'}) = \frac{2n_\infty ze}{\varepsilon\varepsilon_0}\sinh(\frac{ze}{k_bT}\psi) \tag{15}$$

According to the Debye-Hückel approximation, as the surface potential is small , say, $\psi_s << 0.025V$ (Hiemenz and Rajagopalan, 1997), the term $ze\psi/k_bT$ is smaller than unity and the hyperbolic sine function can be approximated as

$$\sinh(\frac{ze\psi}{k_bT}) \approx \frac{ze\psi}{k_bT} \quad \text{for} \quad \frac{ze\psi}{k_bT} << 1 \tag{16}$$

So, the Eq. (15) can be simplified further as

$$\frac{1}{r'}\frac{\partial}{\partial r'}(r'\frac{\partial\psi}{\partial r'}) = \frac{2n_\infty z^2e^2}{\varepsilon\varepsilon_0 k_bT}\psi = \kappa^2\psi \tag{17}$$

where $\kappa^{-1} = (\frac{\varepsilon\varepsilon_0 k_bT}{2n_\infty z^2e^2})^{1/2}$ is the Debye length defined as the thickness of EDL.

Eq. (17) can be numerically solved by the additional boundary conditions

$$\psi(r'=r_s) = \psi_s \quad \text{and} \quad \psi(r'=\infty) = 0$$

where r_s is the radius of the cell and ψ_s is the surface potential at $r'=r_s$.

After the external electrical potential ϕ and the surface potential distribution ψ are found, the total electric potential $\mathbf{\Psi}$ and the net charge distribution can be achieved.

Flow Field

Once an electric field is built up, the aqueous solution that contains chondrocytes can be driven to move, which will influence the motion of the charged cell due to viscous drag forces. The basic equations describing the flow field are the continuity equation

$$\nabla\cdot\mathbf{V}_{eo} = 0 \tag{18}$$

and the momentum equation (Navier-Stokes equation)

$$\rho[\frac{\partial\mathbf{V}_{eo}}{\partial t} + (\mathbf{V}_{eo}\cdot\nabla)\mathbf{V}_{eo}] = -\nabla\mathbf{P} + \mu\nabla^2\mathbf{V}_{eo} + \rho_e\mathbf{E} \tag{19}$$

where $\mathbf{V}_{eo}$ is the bulk electroosmotic velocity vector, ρ is the density of the liquid, $\mathbf{P}$ is the pressure, and μ is the liquid viscosity which can be obtained experimentally.

As mentioned above, the driving force in the liquid flow is the electric force $\rho_e\mathbf{E}$, which appears as the third term of the right hand side of Eq. (19). The electroosmotic flow here is approximated as steady state. So, in Cylindrical Coordinates (r,θ,z), Eqs. (18) and (19) can be rewritten as [11]

$$\nabla\cdot\mathbf{V}_{eo} = \frac{1}{r}\frac{\partial}{\partial r}(rv_{eor}) + \frac{\partial v_{eo\theta}}{\partial\theta} + \frac{\partial v_{eoz}}{\partial z} = 0 \tag{20}$$

$$\begin{aligned}
&v_{eor}\frac{\partial v_{eor}}{\partial r} + \frac{v_{eo\theta}}{r}\frac{\partial v_{eor}}{\partial\theta} - \frac{v_{eo\theta}^2}{r} + v_{eoz}\frac{\partial v_{eor}}{\partial z} \\
&= -\frac{1}{\rho}\frac{\partial P}{\partial r} + \upsilon[\frac{\partial}{\partial r}(\frac{1}{r}\frac{\partial}{\partial r}(rv_{eor})) + \frac{1}{r^2}\frac{\partial^2 v_{eor}}{\partial\theta^2} + \frac{\partial v_{eor}^2}{\partial z^2} \\
&- \frac{2}{r^2}\frac{\partial v_{eo\theta}}{\partial\theta}] + \frac{\rho_e E_r}{\rho} \\
&v_{eor}\frac{\partial v_{eo\theta}}{\partial r} + \frac{v_{eo\theta}}{r}\frac{\partial v_{eo\theta}}{\partial\theta} - \frac{v_{eor}v_{eo\theta}}{r} + v_{eoz}\frac{\partial v_{eo\theta}}{\partial z} \\
&= -\frac{1}{\rho r}\frac{\partial P}{\partial\theta} + \upsilon[\frac{\partial}{\partial r}(\frac{1}{r}\frac{\partial}{\partial r}(rv_{eo\theta})) + \frac{1}{r^2}\frac{\partial^2 v_{eo\theta}}{\partial\theta^2} + \frac{\partial v_{eo\theta}^2}{\partial z^2} \\
&+ \frac{2}{r^2}\frac{\partial v_{eor}}{\partial\theta}] + \frac{\rho_e E_\theta}{\rho} \\
&v_{eor}\frac{\partial v_{eoz}}{\partial r} + \frac{v_{eo\theta}}{r}\frac{\partial v_{eoz}}{\partial\theta} + v_{eoz}\frac{\partial v_{eoz}}{\partial z} \\
&= -\frac{1}{\rho}\frac{\partial P}{\partial z} + \upsilon[\frac{1}{r}\frac{\partial}{\partial r}(r\frac{\partial v_{eoz}}{\partial r}) + \frac{1}{r^2}\frac{\partial^2 v_{eoz}}{\partial\theta^2} + \frac{\partial v_{eoz}^2}{\partial z^2}] \\
&+ \frac{\rho_e E_z}{\rho}
\end{aligned} \tag{21}$$

where v_{eor}, $v_{eo\theta}$ and v_{eoz} are the electroosmotic velocity component in the r, θ, z directions, respectively and $\upsilon = \mu / \rho$ is the kinematical viscosity.

Consider the plane of dish parallel to the coils, it is assumed the boundary conditions for Eqs. (20) and (21) are

$$\frac{\partial v_{eor}}{\partial z} = 0, \frac{\partial v_{eo\theta}}{\partial z} = 0, v_{eoz} = 0, \frac{\partial P}{\partial z} = 0$$

Thus, Eqs. (20) and (21) can be rewritten, respectively, as

$$\frac{1}{r}\frac{\partial}{\partial r}(r v_{eor}) + \frac{\partial v_{eo\theta}}{\partial \theta} = 0 \tag{22}$$

$$v_{eor}\frac{\partial v_{eor}}{\partial r} + \frac{v_{eo\theta}}{r}\frac{\partial v_{eor}}{\partial \theta} - \frac{v_{eo\theta}^2}{r}$$
$$= -\frac{1}{\rho}\frac{\partial P}{\partial r} + \upsilon[\frac{\partial}{\partial r}(\frac{1}{r}\frac{\partial}{\partial r}(r v_{eor})) + \frac{1}{r^2}\frac{\partial^2 v_{eor}}{\partial \theta^2} - \frac{2}{r^2}\frac{\partial v_{eo\theta}}{\partial \theta}]$$
$$v_{eor}\frac{\partial v_{eo\theta}}{\partial r} + \frac{v_{eo\theta}}{r}\frac{\partial v_{eo\theta}}{\partial \theta} - \frac{v_{eor} v_{eo\theta}}{r}$$
$$= -\frac{1}{\rho r}\frac{\partial P}{\partial \theta} + \upsilon[\frac{\partial}{\partial r}(\frac{1}{r}\frac{\partial}{\partial r}(r v_{eo\theta})) + \frac{1}{r^2}\frac{\partial^2 v_{eo\theta}}{\partial \theta^2} + \frac{2}{r^2}\frac{\partial v_{eor}}{\partial \theta}]$$
$$+ \frac{\rho_e m r}{2\rho} \tag{23}$$

Eqs. (22) and (23) can be solved by the additional boundary condition

$$v_{eor}(r = R_{dish}) = 0$$

where R_{dish} is the radius of the culture dish.

Thus, the bulk electroosmotic velocity field can be achieved.

Single Particle Motion

The motion of a single particle is the focus for the growth and migration of chondrocytes. It consists of both the translational and rotational motion.

Consider one chondrocyte in the culture dish where the surrounding solution is assumed to be neutral. Under the electric field induced by PEMF, the solution will not move due to no net charge while the chondrocyte will move because of electrophoresis. In this case, the electric force $\mathbf{F}_E$ has an opposite direction to the electric field **E** as the cell is negatively charged. At the beginning, the hydrodynamic force $\mathbf{F}_h$ has the same direction with **E** but opposite to that of velocity $\mathbf{V}_p$ and $\mathbf{F}_h$ is smaller than $\mathbf{F}_E$, as shown in Fig 5. Thus, the chondrocyte will be accelerated until forces are balanced.

It's well known that Newton's second law governs the motion of particle. The translational motion can be described as

$$m_p \frac{d\mathbf{V}_p}{dt} = \mathbf{F}_E + \mathbf{F}_h \tag{24}$$

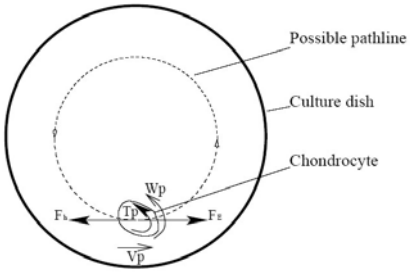

Fig 5: Schematic of a charged cell in motion inside a culture dish under the influence of PEMF

where m_p is the mass of the particle, $\mathbf{V}_p$ is the translational velocity, $\mathbf{F}_E$ is the electrostatic force acting on the charged cell by **E** and $\mathbf{F}_h$ is the hydrodynamic force exerted by the surrounding fluid due to viscous effect. The electrostatic force $\mathbf{F}_E$ can be obtained by

$$\mathbf{F}_E = \rho_e \mathbf{E} \tag{25}$$

and the hydrodynamic force $\mathbf{F}_h$ by

$$\mathbf{F}_h = -\int (\mathbf{n}\cdot\mathbf{p} - \mathbf{n}\cdot\boldsymbol{\tau}) dS \tag{26}$$

where $\mathbf{n}$ is the normal vector pointing outward the drag force, **p** is the pressure and $\boldsymbol{\tau}$ is the viscous stress tensor.

Since the magnitude of electric field increases with the radius of the concentric circle, the electric forces exerted on the chondrocyte surface is not uniform, inducing a torque $\mathbf{T}_p$ which produce a rotation $\mathbf{w}_p$ along its own axis. The rotational motion of the chondrocyte is governed by

$$\mathbf{J}\frac{d\mathbf{w}_p}{dt} = \mathbf{T}_p \tag{27}$$

where $\mathbf{w}_p$ is the angular velocity, $\mathbf{J}$ is the moment of inertia of the particle and $\mathbf{T}_p$ is the torque on the particle (about the center of particle) by the flow field and the nonuniform electric potential.

It's assumed that the shape of chondrocyte can be approximated as a circle. Therefore, the moment of inertia $\mathbf{J}$ can be obtained by

$$\mathbf{J} = \int r^2 dm = \int_0^r r^2 \rho_{cell} 2\pi r dr = \frac{\rho_{cell}}{2}\pi r^4 \tag{28}$$

and the torque about the center of particle $\mathbf{T}_p$ by

$$\mathbf{T}_p = (\sum \mathbf{F}_E + \sum \mathbf{F}_h)\cdot \mathbf{r} \tag{29}$$

where $\mathbf{F}_E$ and $\mathbf{F}_h$ are the electrostatic force and hydrodynamic force respectively and $\mathbf{r}$ is the radius vector of the chondrocyte.

After the translational velocity $\mathbf{V}_p$ and the angular velocity $\mathbf{w}_p$ of the particle are found, the migration of the chondrocyte can be predicted.

Concentration Field

In addition to the motion of a single particle, the concentration distribution of chondrocytes is another important

focus. According to the conservation law of mass, the concentration distribution can be described as [12, 13]

$$\frac{\partial C_i}{\partial t} + (\mathbf{V}_{eo} + \mathbf{V}_{epi}) \cdot \nabla C_i = D_i \nabla^2 C_i + R_i \qquad (30)$$

where C_i is the concentration of the *i*th species, D_i is the diffusion coefficient of the *i*th species, R_i is source or sink term, and $\mathbf{V}_{eo}$ and $\mathbf{V}_{epi}$ are the electroosmotic and electrophoretic velocity vectors, respectively. $\mathbf{V}_{eo}$ can be obtained by Eqs. (18) and (19) and $\mathbf{V}_{epi} = \mathbf{E}\mu_{epi}$, where μ_{epi} is the electrophoretic mobility, which can be measured experimentally by investigating the motion of a single particle in the solution under PEMF [14].

The objective of the investigation is to control the migration of chondrocytes by PEMF through an induced electric field; that is, the distribution of cells. The migration of chondrocytes in the solution depends on the electric field, diffusion coefficient, electrophoretic mobility, geometry of the cells and the properties of the solution around them. Preliminary migration experimental result for chondrocytes is shown in Fig. 6, by an externally applied electric field at a 15 minute interval.

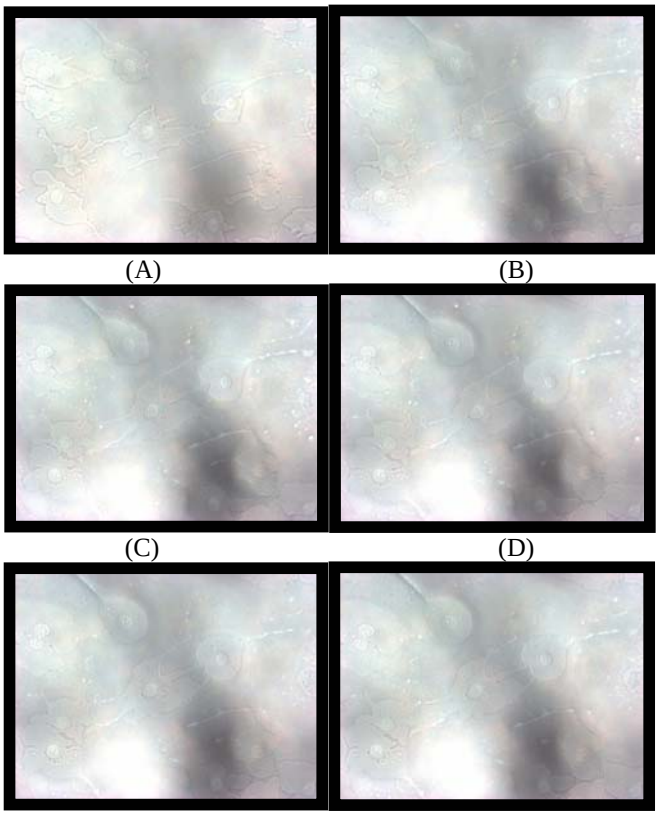

Fig 6 (A-F): Schematic of a series photos at 15 minute intervals which show the migration of chondrocytes

III. Summary

In this paper, a theoretical model is developed to simulate the regeneration of articular cartilage for Osteoarthritis by pulsed electromagnetic fields (PEMF). The chondrocytes, the negatively charged cells in the articular cartilage are driven to move through the induced electric field generated by the two Helmholtz coils, due to the EDL formed between the cells and the surrounding fluid. Thus, electrokinetic phenomena, Electroosmosis (EO) and Electrophoresis (EP), occur during the growth and migration of chondrocytes.

In the simulation, the electrical field, flow field, single particle motion and concentration field are obtained by solving the theoretical model numerically, which accounts for cell distribution in the culture dish. Several approximations are employed to simply the mathematical model and boundary conditions are required to solve these sets of equations numerically.

In addition, our preliminary results from *in vitro* experiments that the use of PEMF appears to be an effective way to control the migration of chondrocytes. The movement of cells can be seen in a series of photos taken at a 15 minute interval, under a 2.8mT amplitude of magnetic field used in experiment.

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