Mathematical Model for Tissue Engineered Intervertebral Disc as a Saturated Porous Media

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Abstract: - Success of the intervertebral disc tissue engineering approach depends on the restoration of its mechanical function and proposing a suitable model as an infrastructure for a better understanding of its mechanobiological behavior is a major requirement. This paper presents a finite element formulation including the chemical behaviour, inertia terms and viscoelasticity which can be used in our predicted tissue engineering procedure as a powerful model. After derivation of the governmental equations, implicit time integration schemes are applied to solve the nonlinear equations. The formulation accuracy and convergence for 1D case are examined with Sun's and Simon's analytical solution and Drost's experimental Data. It is shown that the mathematical model is in excellent agreement and can be used for simulation of the IVD response under different types of mechanical and electrochemical loading conditions.

Key-Words: - Mechanobiology, Finite element, Porous media, Intervertebral disc, Tissue engineering

1 Introduction

The intervertebral disc can be described as a charged, hydrated and permeable material which is comprised largely of collagen and elastic fibers embedded in a proteoglycan gel to form a solid matrix. As an infrastructure for studying the biomechanics of the intervertebral disc tissue engineering, it is so vital to propose suitable mechanobiological models. During the last decade, several researches have been proposed the multiphasic computational models to study mechanics of the soft tissues (such as articular cartilage, intervertebral disc, vascular vessel and skin). Mow et al. [1] first presented the biphasic theory in which the material was modeled as a mixture of two distinct phases and later it was extended by Spilker et al. [2]. On the basis of the Biot theorem, Simon et al. [3, 4] considered the soft tissues in the spinal motion segment as poroelastic materials which was later extended by Yang et al.[5]. Since significant deformations resulting from loading and inherent swelling mechanisms in the soft tissues have been described, Mow et al. [6] developed a triphasic model to consider the effects of swelling and transport in descriptions of soft tissue mechanics. Then Gu et al. [7] and Sun et al. [8] extended triphasic theory to model the mechano-electrochemical behaviors of charged hydrated soft tissues containing electrolytes. Later, Simon et al. [9, 10] and Laible et al. [11, 12] extended poroelastic model to poroelastic transport swelling model which includes chemical effects.

It is so clear that all these models tried to incorporate the features of actual biological tissue but there are some limitations that should be improved for better understanding of the intervertebral disc biomechanics. Except for the model of Simon [3, 4] and Yang [5], the previous models are quasi static which means that the inertia is ignored. Actually, the inertia terms can be significant when the external forces vary rapidly. Also the construction of biological tissue such as collagen fibers and proteoglycan gel are highly viscoelastic, but only the models of Huang [13], Suh [14], and Yang [5] considered this point. Additionally, some limited models considered the chemical and electrical effects (Sun [8], Simon [9, 10] and Iatridis [12]), which is so important for us in our predicted tissue engineering procedure. So based on the work of Sun, Simon and Yang, this paper presents a novel mixed finite element formulation including the chemical behaviour, inertia terms and viscoelasticity which can simulate intervertebral disc response regarding to the different types of mechanical, electrical and physicochemical loading conditions.

2 Mechanobiological Model

This mechanobiological model considers a charged hydrated tissue engineered intervertebral disc as a mixture consisting of: (1) a porous, permeable, charged solid phase; (2) an incompressible fluid phase; and (3) ion phase with two ion species, i.e.,

anion and cation. According to the Biot theory, the derivation of the governing equation of the fluid was based on empirical evidence that the fluid flow in porous media obeys Darcy's law [10]. By the way, this model is strictly based on the laws of continuum mechanics.

2.1 Porous Model

There are different forces on the solid phase which are the frictional force between solid and fluid, body force, fluid pressure and the pressure due to the chemical potential. So the momentum conservation law for the porous solid in the absence of body force can be written as Eq.1.

$$\frac{\partial T_{ji}}{\partial X_j} - \rho_s \ddot{u}_i - n\rho_f (J^{-1}\frac{\partial x_i}{\partial X_j})\ddot{w}_j = 0 \tag{1}$$

As the model satisfies the Darcy equation, the momentum conservation laws for the pore fluid in the absence of body force can be written as Eq.2 [9, 10].

$$\frac{\partial (p + \frac{p^c}{n})}{\partial X_i} - \frac{n}{k}\dot{w}_j - \rho_f \frac{\partial x_j}{\partial X_i}\ddot{u}_j - \rho_f (J^{-1}\frac{\partial x_k}{\partial X_i}\frac{\partial x_k}{\partial X_j})\ddot{w}_j = 0 \tag{2}$$

The storage due to compressibility of the solid and of the fluid should be equal to the dilation of the fluid and of the solid (On the basis of the mass conservation law). So the fluid pressure can be expressed as Eq.3 [3].

$$p = nQw_{i,i} + \alpha QJ[\frac{\partial X_r}{\partial x_k}E_{rs}\frac{\partial X_s}{\partial x_k}] \tag{3}$$

Where: Q and α are as Eqs.4 and 5.

$$\frac{1}{Q} = \frac{n}{K_{fluid}} + \frac{\alpha - n}{K_{Solid}} \tag{4}$$

$$\alpha = 1 - \frac{K}{K_{solid}} \tag{5}$$

2.2 Electrochemical Model

On the basis of Sun's work [8] (in the absence of the magnetic and gravitational effects), the governmental equations can be derived from the momentum equations, continuity equations and electrical current condition as Eqs.6 and 7.

$$\nabla \cdot \mathbf{J}^+ - \nabla \cdot \mathbf{J}^- = 0 \tag{6}$$

$$\frac{\partial c^k}{\partial t} + \nabla \cdot \mathbf{J}^+ + \nabla \cdot \mathbf{J}^- + \nabla \cdot (c^k \mathbf{v}^s) = 0 \tag{7}$$

Where,

$$\mathbf{J}^+ = -\frac{\rho^+ c^+ \nabla\tilde{\mu}^+ (f_{-sf} + f_{-+}) + \rho^- c^+ \nabla\tilde{\mu}^- f_{+-}}{f_{+sf}f_{-sf} + f_{+sf}f_{-+} + f_{+-}f_{-sf}} \tag{8}$$

$$\mathbf{J}^- = -\frac{\rho^- c^- \nabla\tilde{\mu}^- (f_{+sf} + f_{+-}) + \rho^+ c^- \nabla\tilde{\mu}^+ f_{-+}}{f_{+sf}f_{-sf} + f_{+sf}f_{-+} + f_{+-}f_{-sf}} \tag{9}$$

We can rewrite the Eqs.8 and 9 in Eqs.10 and 11 by nominating k_β^α as Eqs.12-15

$$\mathbf{J}^+ = k_1^+ c^+ \nabla\tilde{\mu}^+ + k_2^+ c^+ \nabla\tilde{\mu}^- \tag{10}$$

$$\mathbf{J}^- = k_1^- c^- \nabla\tilde{\mu}^- + k_2^- c^- \nabla\tilde{\mu}^+ \tag{11}$$

$$k_1^+ = -\frac{\rho^+ (f_{-sf} + f_{-+})}{f_{+sf}f_{-sf} + f_{+sf}f_{-+} + f_{+-}f_{-sf}} \tag{12}$$

$$k_2^+ = -\frac{\rho^- f_{+-}}{f_{+sf}f_{-sf} + f_{+sf}f_{-+} + f_{+-}f_{-sf}} \tag{13}$$

$$k_1^- = -\frac{\rho^- (f_{+sf} + f_{+-})}{f_{+sf}f_{-sf} + f_{+sf}f_{-+} + f_{+-}f_{-sf}} \tag{14}$$

$$k_2^- = -\frac{\rho^+ f_{-+}}{f_{+sf}f_{-sf} + f_{+sf}f_{-+} + f_{+-}f_{-sf}} \tag{15}$$

3 FE Formulation of the Model

Using the standard Galerkin weighted residual method the finite element formulation is constructed [15]. Applying the divergence and green's theorem, the finite element formulation of the porous and electrochemical model is derived in matrix form as Eqs.16, 17 and 18.

$$\begin{bmatrix} \mathbf{M_{11}} & \mathbf{M_{12}} & \mathbf{0} \\ \mathbf{M_{21}} & \mathbf{M_{22}} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \end{bmatrix} \begin{bmatrix} \ddot{\mathbf{u}} \\ \ddot{\mathbf{w}} \\ \ddot{\mathbf{p}} \end{bmatrix} + \begin{bmatrix} \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{C_{22}} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \end{bmatrix} \begin{bmatrix} \dot{\mathbf{u}} \\ \dot{\mathbf{w}} \\ \dot{\mathbf{p}} \end{bmatrix} = \begin{bmatrix} \mathbf{f_1} \\ \mathbf{f_2} \\ \mathbf{f_3} \end{bmatrix} \tag{16}$$

$$\mathbf{K}^+\tilde{\boldsymbol{\mu}}^+ + \mathbf{K}^-\tilde{\boldsymbol{\mu}}^- = \mathbf{f_4} \tag{17}$$

$$\mathbf{C^c}\dot{\mathbf{c}} = \mathbf{f_5} \tag{18}$$

Where: the mentioned parameters are defined according to the Eqs.19-31.

$$\mathbf{M_{11}} = \int_\Omega \rho_s N_{mi}^u N_{ni}^u d\Omega \tag{19}$$

$$\mathbf{M_{12}} = \int_\Omega N_{mi}^u n\rho_f (J^{-1}\frac{\partial x_i}{\partial X_j})N_{nj}^w d\Omega \tag{20}$$

$$\mathbf{M_{21}} = \int_\Omega N_{mi}^w \rho_f \frac{\partial x_j}{\partial X_i} N_{nj}^w d\Omega \tag{21}$$

$$\mathbf{M_{22}} = \int_\Omega N_{mi}^w \frac{\rho_f}{J}\frac{\partial x_k}{\partial X_i}\frac{\partial x_k}{\partial X_j} N_{nj}^w d\Omega \tag{22}$$

$$\mathbf{C_{22}} = \int_\Omega \frac{n}{k} N_{mi}^w N_{ni}^w d\Omega \tag{23}$$

$$\mathbf{f_1} = \int_{\partial\Omega} N_{mi}^u t_i ds - \int_\Omega N_{mi,j}^{u^T} \mathbf{T} d\Omega \tag{24}$$

$$\mathbf{f_2} = \int_\Omega N^w_{mi} N^w_{ni} \cdot p_n d\Omega + \int_\Omega N^w_{mi} \frac{p^c{}_{,i}}{n} d\Omega \tag{25}$$

$$\mathbf{f_3} = \int_\Omega N^p_m N^p_n d\Omega p - \int_\Omega (nQw_{i,i} + \alpha QJ[\frac{\partial X_r}{\partial x_k} E_{rs} \frac{\partial X_s}{\partial x_k}])_n N^p_m d\Omega \tag{26}$$

$$\mathbf{K}^+ = \int_\Omega (-k_1^+ c^+ + k_2^- c^-)(\nabla N^c) \cdot (\nabla N^c) d\Omega \tag{27}$$

$$\mathbf{K}^- = \int_\Omega (-k_2^+ c^+ + k_1^- c^-)(\nabla N^c) \cdot (\nabla N^c) d\Omega \tag{28}$$

$$\mathbf{f_4} = -\int_\Omega (k_1^+ c^+ \nabla \tilde{\mu}^+ N^c + k_2^+ c^+ \nabla \tilde{\mu}^- N^c - k_1^- c^- \nabla \tilde{\mu}^- N^c - k_2^- c^- \nabla \tilde{\mu}^+ N^c) \cdot \mathbf{n} ds \tag{29}$$

$$\mathbf{C^c} = \int_\Omega N^{cT} N^c d\Omega \tag{30}$$

$$\mathbf{f_5} = -\int_\Omega (k_1^+ c^+ \nabla \tilde{\mu}^+ N^c + k_2^+ c^+ \nabla \tilde{\mu}^- N^c + k_1^- c^- \nabla \tilde{\mu}^- N^c + k_2^- c^- \nabla \tilde{\mu}^+ N^c) \cdot \mathbf{n} ds + \int_\Omega (k_1^+ c^+ + k_2^- c^-)(\nabla N^c) \cdot (\nabla N^c) d\Omega \cdot \tilde{\mu}^+ + \int_\Omega (k_2^+ c^+ + k_1^- c^-)(\nabla N^c) \cdot (\nabla N^c) d\Omega \cdot \tilde{\mu}^- - \int_s (c^k \mathbf{v}^s N^c) \cdot \mathbf{n} ds + \int_\Omega (\nabla N^c) \cdot (c^k \mathbf{v}^s) d\Omega \tag{31}$$

4 Numerical Solution

The implicit Newmark integration scheme [15, 16] is applied to solve Eq.16. In this method assumptions are as Eqs.32 and 33.

$${}^{t+\Delta t}\dot{\mathbf{X}} = {}^t\dot{\mathbf{X}} + [(1-\delta){}^t\ddot{\mathbf{X}} + \delta {}^{t+\Delta t}\ddot{\mathbf{X}}]\Delta t \tag{32}$$

$${}^{t+\Delta t}\mathbf{X} = {}^t\mathbf{X} + {}^t\dot{\mathbf{X}}\Delta t + [(\frac{1}{2}-\alpha){}^t\ddot{\mathbf{X}} + \alpha {}^{t+\Delta t}\ddot{\mathbf{X}}]\Delta t^2 \tag{33}$$

Where α and δ are parameters that can be determined to obtain integration accuracy and stability. A very common technique used is the trapezoidal rule, which is Newmark method with $\delta = \frac{1}{2}$ and $\alpha = \frac{1}{4}$, and we use this method to demonstrate the basic additional consideration involved in a nonlinear analysis.

So we can rewrite the Eqs.32 and 33 as Eqs.34 and 35,

$${}^{t+\Delta t}\dot{\mathbf{X}} = {}^t\dot{\mathbf{X}} + \frac{1}{2}[{}^t\ddot{\mathbf{X}} + {}^{t+\Delta t}\ddot{\mathbf{X}}]\Delta t \tag{34}$$

$${}^{t+\Delta t}\mathbf{X} = {}^t\mathbf{X} + {}^t\dot{\mathbf{X}}\Delta t + \frac{1}{4}[{}^t\ddot{\mathbf{X}} + {}^{t+\Delta t}\ddot{\mathbf{X}}]\Delta t^2 \tag{35}$$

At time $t+\Delta t$, we can write Eq.36 for a dynamic system.

$$\mathbf{M}{}^{t+\Delta t}\ddot{\mathbf{X}} + \mathbf{C}{}^{t+\Delta t}\dot{\mathbf{X}} = {}^{t+\Delta t}\mathbf{F} \tag{36}$$

Elimination ${}^{t+\Delta t}\ddot{\mathbf{X}}$ and ${}^{t+\Delta t}\dot{\mathbf{X}}$ by using Eqs.34 to 36, gives Eq.37

$$[\frac{4}{\Delta t^2}\mathbf{M} + \frac{2}{\Delta t}\mathbf{C}]{}^{t+\Delta t}\mathbf{X} = {}^{t+\Delta t}\mathbf{F} + [\frac{4}{\Delta t^2}{}^t\mathbf{X} + \frac{4}{\Delta t}{}^t\dot{\mathbf{X}} + {}^t\ddot{\mathbf{X}}]\mathbf{M} + [\frac{2}{\Delta t}{}^t\mathbf{X} + {}^t\dot{\mathbf{X}}]\mathbf{C} \tag{37}$$

So the term ${}^{t+\Delta t}\dot{\mathbf{X}}$ and ${}^{t+\Delta t}\ddot{\mathbf{X}}$ can be updated as Eq.38 and 39.

$${}^{t+\Delta t}\dot{\mathbf{X}} = \frac{2}{\Delta t}({}^{t+\Delta t}\mathbf{X} - {}^t\mathbf{X}) - {}^t\dot{\mathbf{X}} \tag{38}$$

$${}^{t+\Delta t}\ddot{\mathbf{X}} = \frac{4}{\Delta t^2}({}^{t+\Delta t}\mathbf{X} - {}^t\mathbf{X} - \Delta t {}^t\dot{\mathbf{X}}) - {}^t\ddot{\mathbf{X}} \tag{39}$$

It is clear that ${}^t\dot{\mathbf{X}}$ and ${}^t\ddot{\mathbf{X}}$ are known from the previous step of the calculations. So if ${}^{t+\Delta t}\mathbf{X}$ is determined from Eq.37, ${}^{t+\Delta t}\dot{\mathbf{X}}$ and ${}^{t+\Delta t}\ddot{\mathbf{X}}$ can be obtained from equations 38 and 39. So, the main point of this problem is to solve Eq.37. The Newton method was used for solving Eq.37.

The implicit backward-Euler method [15, 16] is applied to solve Eqs.17 and 18. This method approximates the derivative as Eqs.40

$${}^{t+\Delta t}\dot{X} = \frac{1}{\Delta t}({}^{t+\Delta t}X - {}^{(t)}X) \tag{40}$$

So Eqs.17 and 18 become as Eqs.41 and 42,

$${}^{(t+\Delta t)}\mathbf{K}^+ {}^{(t+\Delta t)}\tilde{\boldsymbol{\mu}}^+ + {}^{(t+\Delta t)}\mathbf{K}^- {}^{(t+\Delta t)}\tilde{\boldsymbol{\mu}}^- = {}^{(t+\Delta t)}\mathbf{f_4} \tag{41}$$

$$\frac{\mathbf{C^c}}{\Delta t}({}^{(t+\Delta t)}\mathbf{c} - {}^{(t)}\mathbf{c}) = {}^{(t+\Delta t)}\mathbf{f_5} \tag{42}$$

The Newton method was used for solving Eqs.41 and 42.

5 Validation

To investigate the validation of the porous model, Simon's one-dimensional poroelastic problem with analytical solution [3, 4] is used. This problem represents the motion of a porous elastic material along the x-axis. The material properties, initial and boundary conditions are referred to Simon's work [3, 4]. The shape function used in this one-dimensional problem is isoparametric linear function (Ten elements). Fig.1 shows how the solid and fluid displacements vary with time at x=0.

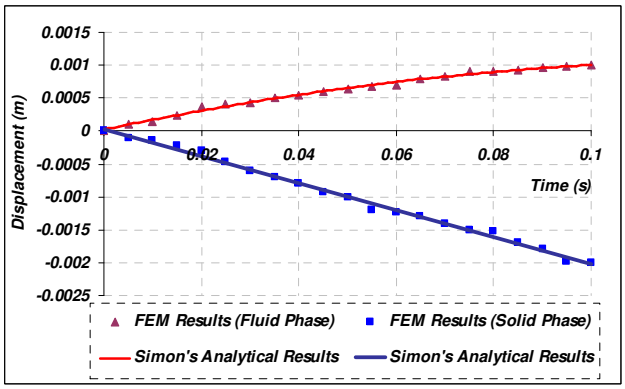

Fig. 1: Validation of the model with Simon's work

To validate the mechano-electrochemical phenomena of charged, hydrated intervertebral disc,

a transient free swelling problem was studied using our finite element formulation in compare with Sun's results [8]. The shape functions used in this one-dimensional problem are isoparametric linear functions (five elements). Assuming a frictionless lateral boundary, only axial motion is possible and the problem is reduced to a 1-D problem. The material properties, initial and boundary conditions are referred to Sun's work [8]. Fig.2 shows the history of the solid displacement at the surface.

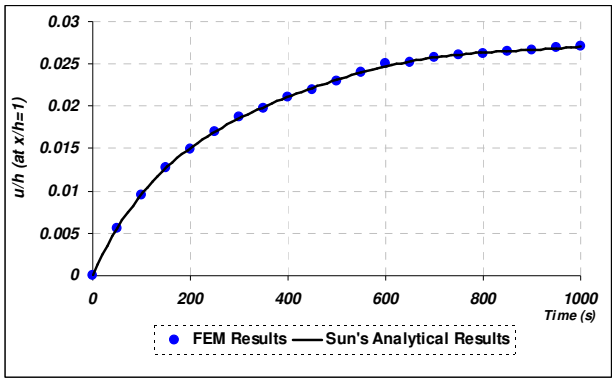

Fig. 2: Validation of the model with Sun's work (Free Swelling Problem)

After validation of the FEM results with analytical solutions, our model was used to simulate the load displacement response as obtained by Drost et al. [17]. That study considered the compression of the canine annulus under chemical and mechanical loading. Using our FEM model, the mentioned experimental test was simulated in following load stages:

(1) Conditioning, c=0.6 M, P= 0.08 MPa
(2) Swelling, c=0.2 M, P=0.08 MPa
(3) Consolidation, c=0.2 M, P=0.20 MPa.

Fig.3 shows how the Displacement of annulus fibrosus specimen varies with time and compares theoretical results with experimental data (by Drost et al. [17]).

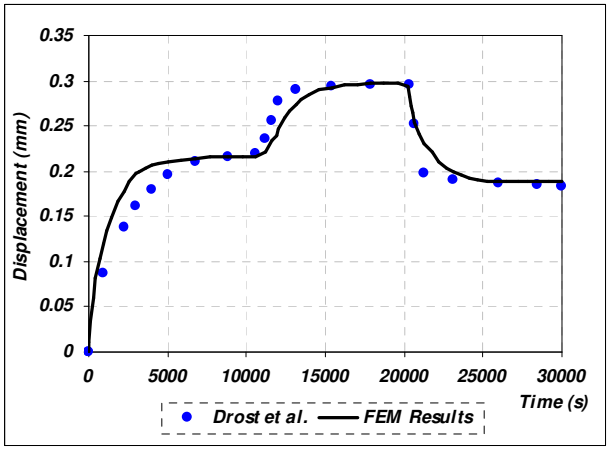

Fig. 3: Validation of the model with Drost's Experimental Data

However, the formulation accuracy and convergence for 1D case are examined and it is shown that the FEM results are in excellent agreement.

6 Conclusion

Success of the intervertebral disc tissue engineering approach depends on the restoration of its mechanical function and proposing a suitable model as an infrastructure for a better understanding of its mechanobiological behavior is a major requirement. Based on the importance of considering the viscoelasticity, inertia terms and electro chemical behaviour in modeling the biomechanical responses of the tissue engineering procedure, we developed our mathematical formulation. The standard Galerkin weighted residual method was used for providing numerical solution to this problem (which is intractable to analytic solution) and then implicit time integration schemes are applied to solve the nonlinear equations.

Our model was verified by comparison of the derived finite element results for one dimensional model with analytical solution by Simon et al. [3, 4] and Sun et al. [8] and also experimental data by Drost et al. [17]. It is shown that our finite element formulation is capable of solving the triphasic problems of intervertebral disc under different types of mechanical, electrical and physicochemical loading conditions. Now on the basis of this infrastructure model we can devote our future work to development of this model in details and studying the mechanobiology of the tissue engineered intervertebral disc.

Nomenclature

c	Concentration of the ion phase
$\mathbf{E}$	Strain Tensor
$f_{\alpha\beta}$	Frictional coefficients between components in multiphasic model
J	Jacobean Matrix
$\mathbf{J}^+ / \mathbf{J}^-$	Positive / negative ion flux
k	Permeability
K_s / K_f	Bulk module for the solid / fluid phases
$\mathbf{K}$	Stiffness matrix
n	Porosity
N^i	Shape functions
P	Fluid pressure
p^c	Pressure due to the chemical potential
$\mathbf{T}$	Stress Tensor
t_i	Pressure at the boundary
$\mathbf{u}$	Displacement of solid
$\mathbf{v}^\alpha$	Velocity of α component

$\mathbf{w}$	Relative displacement of fluid
μ^+/μ^-	Electrochemical potentials for Cation / Anion
μ_0	Initial chemical potential
ρ_α	Mass density of α component

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