THE MECHANO-ELECTROCHEMICAL ENVIRONMENT OF CHONDROCYTES IN ARTICULAR CARTILAGE EXPLANTS UNDER UNCONFINED COMPRESSION: EMPHASIS ON THE CELL-MATRIX INTERACTIONS

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INTRODUCTION

The mechanical and electrochemical (MEC) environments, such as stress, strain, fluid and osmotic pressures, and electrical potential, have been reported to modulate the biosynthetic activities of chondrocytes within articular cartilage [1, 2]. However, the specific sequence of events through which the chondrocytes convert mechanical, chemical, and electrical signals to an intracellular biochemical response is not fully understood because few studies are available that describe the MEC fields. Without in-depth analyses of the MEC environment around chondrocytes, the interactions between the chondrocytes and the extracellular matrix (ECM) cannot be determined. Such knowledge could significantly enhance our understanding of the MEC signal-transduction mechanism(s) of the chondrocytes in the tissue.

Computational models of cell-matrix interactions have been proposed to analyze the MEC environment around chondrocytes. Such fields depend on not only the composition and properties of the tissue, but also on the location of the cell within the ECM as well as the manner of loading. As a first step, a finite element model (FEM) based on the biphasic theory was used to study the mechanical environment of the chondrocyte in cartilage under compression [3]. Subsequently, a FEM of the triphasic theory was proposed to study the MEC environments of these cells in the one-dimensional confined compression configuration [4].

The unconfined compression is a more popular testing configuration due to the ease for the fluid, ion and nutrient transport across the lateral surface of the specimen. However, in the unconfined configuration, it has been shown that a more complex MEC fields is created in the ECM [5]. In the present investigation, we aim to study the comprehensive MEC environments around chondrocytes within articular cartilage under the unconfined compression configuration; the MEC fields around the cells will be calculated to assess the in situ cell-matrix interactions.

METHOD

Based on the triphasic theory [6], a multi-scale finite element model [3, 7] was used to analyze both the ECM and the chondrocytes. Each ws modeled as a triphasic mixture with its individual properties. Each consisted of a charged permeable and deformable solid phase, an interstitial water phase and an ion phase (including cations and anions). At the macroscopic level (~1 mm), a cylindrical cartilage explant was placed between two rigid, frictionless, non-permeable loading platens, and was subjected to a compressive step displacement (surface-to-surface strain ε_0=10%) (Fig. 1a). At the microscopic level (50 μm), the chondrocyte was modeled as a spherical inclusion embedded within and adhered to the ECM of the cartilage explant (Fig. 1b). At the macro-scale, the tissue-level results (the solid displacement, the water chemical potential and the ion electrochemical potentials) were calculated; following the method of [3] on the micro-scale the fields were interpolated onto defined boundaries along the cell-matrix domain from within the tissue, and the FEM computations were then carried out. The cell radius was set to 5 μm and the cell-matrix domain was 50×50 μm. In our current study, the micro-scale cell-matrix model was located at the central axis of the cartilage explant mid-way between the platens. Typical material properties were used for the ECM and the chondrocyte (Table 1).

Table 1. Properties of Cartilage ECM and Chondrocyte

Property	ECM	Chondrocyte
Intrinsic Poisson's Ratio ν_s	0.2	0.35
Intrinsic Young's Modulus E_s	0.36 (MPa)	2.6 (kPa)
Permeability (m^4/Ns)	$1x10^{-15}$	$0.5x10^{-11}$
Porosity ϕ^w_0	0.75	0.9
Fixed Charged Density (mEq/ml)	0.2	0.14

RESULTS AND DISCUSSION

Both cartilage ECM and chondrocyte exhibit time-dependent behaviors due to the time-dependent fluid exudation from the lateral edge of the tissue. The predicted stress, strain, pressure, and electrical fields in the vicinity of the chondrocyte were spatially non-uniform and differed significantly from those in the ECM (Fig 3).

Instantaneously after the load was applied, the tissue expanded laterally like an incompressible single-phase elastic material. The

dilatations of the ECM and the chondrocyte was close to zero at early time steps (Fig 2). As time proceeded, the dilatations of both ECM and the chondrocyte became negative and the magnitude increased due to fluid exudation. The equilibrium compressive volume change in the chondrocyte was found to be –5%, which was twice as large as in the far field ECM (10 times the cell radius). This is due to the significant difference (3 orders of magnitude) in the cell and ECM properties. This important result shows the amplification of the dilatation signals from the tissue level to the cell level.

During the fluid exudation process, fluid pressure was predicted to be non-uniform throughout the explant, and the region near the central axis bore the most significant pressurization. Due to high permeability of the cell, the pressure inside the chondrocyte was nearly uniform with the value close to that in the surrounding ECM (Fig. 3b). This result suggests that the chondrocytes near the central axis of the tissue explant experience the most significant pressurization during the compression.

The electrical potential (relative to external bathing solution) was found to be nearly uniform inside the cell (Fig. 3c), and was not significantly changed with time. This suggests that the cell may not experience significant electrical potential signals during the unconfined compression.

In this study based on the triphasic model for the ECM and cell, and even loaded under such simple condition as the unconfined compression, a clear picture emerged detailing the complex nature of the MEC fields in explants. The results clearly show that non-homogeneous fluid and osmotic pressure, ion and fluid flows, and stress and strain fields will always be developed in the ECM, particularly near the chondrocytes. Clearly simple interpretations "compression induced" modulation of chondrocyte biosynthetic activities belie the complexity of the signal transduction mechanisms in unconfined compression cartilage explant studies. These types of theoretical and computational analyses, together with proper experimental results, are necessary to provide effective method aimed at elucidating the mechano-transduction mechanisms in cartilage.

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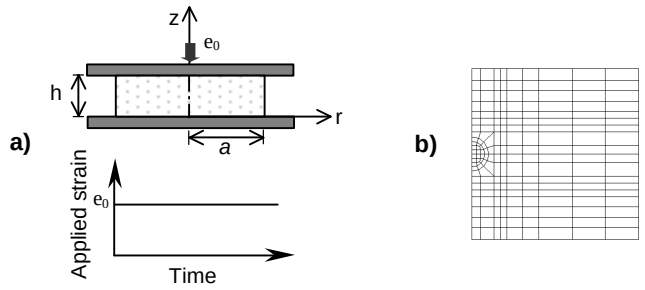

Figure 1. a) Unconfined compression configuration with a step displacement of 10% compressive strain, a=0.75 mm, h=0.5 mm, b) A micro-scale finite element mesh (50x50 μm)

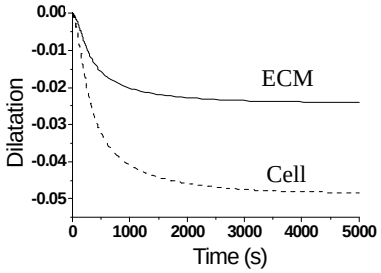

Figure 2. Time history plot of the dilatation at the center of the cell and in the far field ECM (10 times the cell radius)

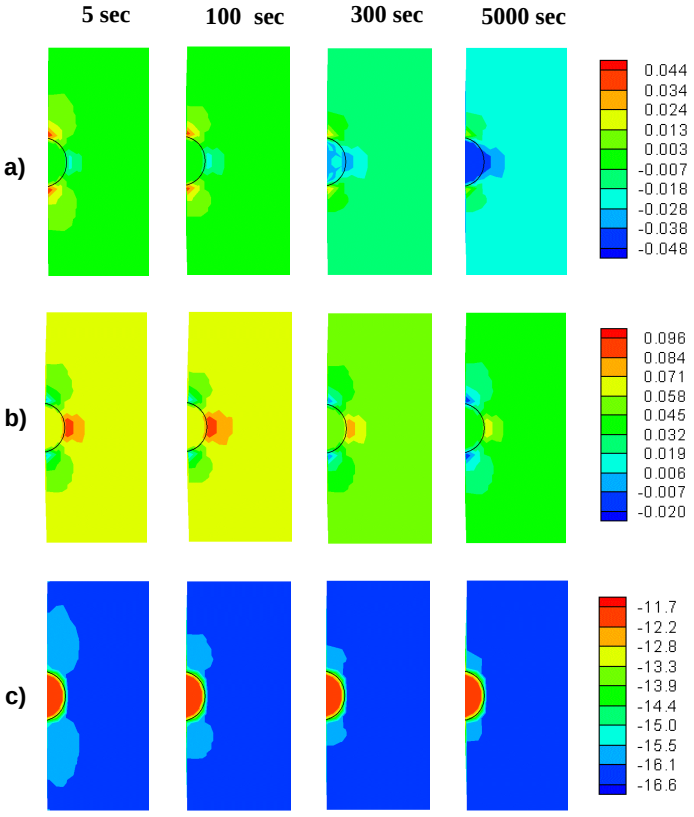

Figure 3. Contour plot of major MEC field results from the micro-scale model, a) Dilatation, b) Pressure (P-P_0, P_0=initial osmotic pressure), normalized by 0.24 MPa, c) Electrical potential (mV)

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