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Cell viability in intervertebral disc under various nutritional and dynamic loading conditions: 3d Finite element analysis

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Abstract

In this study, a new cell density model was developed and incorporated into the formulation of the mechano-electrochemical mixture theory to investigate the effects of deprivation of nutrition supply at boundary source, degeneration, and dynamic loading on the cell viability of intervertebral disc (IVD) using finite element methods. The deprivation of nutrition supply at boundary source was simulated by reduction in nutrition level at CEP and AF boundaries. Cases with 100%, 75%, 60%, 50% and 30% of normal nutrition level at both CEP and AF boundaries were modeled. Unconfined axial sinusoidal dynamic compressions with different combinations of amplitude ($u=10\pm 2.5\%$, $\pm 5\%$) and frequency ($f=1, 10, 20$ cycle/day) were applied. Degenerated IVD was modeled with altered material properties. Cell density decreased substantially with reduction of nutrition level at boundaries. Cell death was initiated primarily near the NP–AF interface on the mid-plane. Dynamic loading did not result in a change in the cell density in non-degenerated IVD, since glucose levels did not fall below the minimum value for cell survival; in degenerated IVDs, we found that increasing frequency and amplitude both resulted in higher cell density, because dynamic compression facilitates the diffusion of nutrients and thus increases the nutrition level around IVD cells. The novel computational model can be used to quantitatively predict both when and where cells start to die within the IVD under various kinds of nutritional and mechanical conditions.

Keywords

Biomechanics; Mechanobiology; Transport phenomena; Nutrition; Glucose concentration; Cell density; Dynamic compression; Mixture theory

1. Introduction

The intervertebral disc (IVD) cells play a vital role in maintaining IVD health and function. Not only do cells synthesize the extracellular matrix (ECM), a significant structure helping sustain the mechanical force for the IVD in the spine, but they also synthesize catabolic molecules responsible for matrix breakdown. A disruption in the delicate balance between

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anabolic and catabolic activities leads to alteration of ECM, which is strongly correlated with structural remodeling, leading to tissue disorganization and, resultantly, IVD dysfunction and degeneration (Adams and Roughley, 2006; Bibby and Urban, 2004).

Degenerative changes to IVD include decreased nutrients levels, reduced cell density, reduced proteoglycan synthesis and alteration in collagen distribution (Maroudas, 1975; Maroudas et al., 1975; Oegema, 1993; Roberts et al., 1989; Urban and Roberts, 2003). Reduction of cell density in degenerated IVD tissue greatly diminishes the ability of the cells to synthesize and maintain the ECM structure, deterioration of which further exacerbates the degeneration of IVD tissues.

Due to the avascular nature of the tissue, essential nutrients (e.g., glucose and oxygen) are transported in and metabolic wastes (e.g., lactic acid) out of the tissue through the dense ECM by diffusion (mainly for small molecules) and convection (mainly for large molecules) from the peripheral and endplate vasculatures. Most of the nucleus pulposus (NP) cells rely on nutrients supplied through the cartilaginous endplate (CEP) route while the cells in the annulus fibrosus (AF) region are mainly nurtured through the annulus peripheral pathway (Bibby and Urban, 2004; Maroudas, 1975; Nachemson et al., 1970; Roberts et al., 1989; Urban and Roberts, 2003; Urban et al., 2000). Adequate nutrient supply has long been regarded as a crucial factor for maintaining normal activities of IVD cells (Bibby et al., 2002; Bibby and Urban, 2004; Horner and Urban, 2001; Nachemson et al., 1970; Oegema, 1993; Urban et al., 2000). It has been shown that the density of IVD cells is mainly dependent on glucose concentration (Bibby et al., 2002; Bibby and Urban, 2004; Horner and Urban, 2001; Jackson et al., 2011a; Shirazi-Adl et al., 2010).

In patients with cigarette smoking, malnutrition, or disorders like blood aneurysms, nutrition levels from the boundary vasculatures tends to decrease accordingly, which could lead to cell death and the development of IVD degeneration (Frymoyer et al., 1983; Gyntelbe, 1974; Holm and Nachemson, 1988). Mechanical loading has been shown not only to directly affect the intrinsic cellular activity (Huang et al., 2004; Kasa et al., 2003; Kroeber et al., 2005; MacLean et al., 2004; Ohshima et al., 1995; Wang et al., 2007; Wuertz et al., 2009), but also to influence the transport of nutrients through the ECM of the IVD tissue (Huang and Gu, 2007; Huang et al., 2012; Jackson et al., 2011b, in press, 2008; Malandrino et al., 2011; Yao and Gu, 2006, 2007; Yuan et al., 2009). Knowledge of changes in cell viability and metabolism in the IVD under various biological, physical and chemical signals is essential for understanding IVD degeneration.

However, it is difficult to study the complicated cellular environment in IVD in vivo experimentally. Numerical methods therefore have been increasingly used to investigate the transport of nutrients and cell viability within the IVDs (Huang and Gu, 2008; Huang et al., 2012; Jackson et al., 2011a; Sélard et al., 2003; Shirazi-Adl et al., 2010; Soukane et al., 2005, 2007, 2009). Shirazi-Adl et al. (2010) were the first to introduce a theoretical model to describe the coupling of cell viability and nutrition level in IVD. In this model (Shirazi-Adl et al., 2010), it is assumed that cell density varies instantaneously with glucose concentration. This model has also been used in our previous study on cell viability in IVD (Jackson et al., 2011a). One of the disadvantages of this model is that the resurrection of dead cells would occur when the glucose level recovers after falling below certain critical level for cell survival (e.g., 0.5 mM (Bibby and Urban, 2004)). Another problem of this model is that it cannot be used to analyze cell viability in a time-dependent process under dynamic situations. In fact, to date, there is no theoretical model that is capable of adequately describing the effect of nutrition levels on cell viability in a time-dependent manner.

Therefore, the objectives of this study were to develop (1) a novel constitutive model for IVD cell viability and (2) a comprehensive numerical tool to analyze and predict how cell viability was affected by the alteration in the extracellular microenvironment that results from disturbances in nutrition deprivation, degeneration, and dynamic loading in the realistic, human IVDs in a time-dependent manner.

2. Theoretical model

The IVD is assumed as a mixture of intrinsically incompressible elastic solid phase (denoted as 's'), water phase (denoted as 'w'), and charged (Na^+ and Cl^-) and uncharged (glucose, oxygen, lactate) solute (denoted as 'a') phases. The governing equations for the mixture are summarized as follows (Ateshian, 2007; Gu et al., 1998; Lai et al., 1991):

$$\nabla \cdot \boldsymbol{\sigma} = 0 \quad (1)$$

$$\nabla \cdot (\mathbf{v}^s + \mathbf{J}^w) = 0 \quad (2)$$

$$\frac{\partial(\phi^w c^a)}{\partial t} + \nabla \cdot (\mathbf{J}^a + \phi^w c^a \mathbf{v}^s) = Q^a \quad (3)$$

where $\boldsymbol{\sigma}$ is the total stress of the mixture, $\mathbf{v}^s$ is the velocity of the solid phase, $\mathbf{J}^w$ is the volume flux of water relative to the solid phase, $\mathbf{J}^a$ is the molar flux of solute a relative to the solid phase, ϕ^w is the water volume fraction (also known as tissue porosity or water content), c^a is the molar concentration (per unit fluid volume) of solute a , and Q^a is the cellular metabolic rate of solute a per unit tissue volume. The total stress $\boldsymbol{\sigma}$, volume flux of water ($\mathbf{J}^w$), and molar flux of solute a ($\mathbf{J}^a$) can be expressed as

$$\boldsymbol{\sigma} = -p\mathbf{I} + \lambda \text{tr}(\mathbf{E})\mathbf{I} + 2\mu\mathbf{E} \quad (4)$$

$$\mathbf{J}^a = H^a c^a \mathbf{J}^w - \frac{D^a \rho^a}{RT} \nabla \tilde{\mu}^a \quad (5)$$

$$\mathbf{J}^w = -k \left(\rho_t^w \nabla \mu^w + \sum_a H^a c^a M^a \nabla \tilde{\mu}^a \right) \quad (6)$$

where p is the fluid pressure, $\mathbf{I}$ is the identity tensor, λ and μ are the Lamé constants of the solid matrix, $\mathbf{E}$ is the infinitesimal strain tensor for the solid matrix, k is the hydraulic permeability, ρ^a is the apparent mass density of solute a , ρ_t^w is the true mass density of water, H^a is the convection coefficient (hindrance factor) of solute a , M^a is the molar weight of solute a , D^a is the diffusivity of solute a , R is the universal gas constant and T is the absolute temperature. The metabolic rates of sodium ion (Na^+) and chloride ion (Cl^-) are assumed to be zero (i.e., $Q^{\text{Na}^+} = Q^{\text{Cl}^-} = 0$). The cellular metabolic rates of oxygen, glucose, and lactate (per unit tissue volume) and pH are given as follows (Bibby et al., 2005; Huang and Gu, 2008; Huang et al., 2012):

$$Q^{\text{O}_2} = -\frac{V'_{\max}(pH-4.95)c^{\text{O}_2}}{K'_m(pH-4.59)+c^{\text{O}_2}} \rho^{\text{cell}} \quad (7)$$

$$Q^{lactate} = \exp(-2.47 + 0.93pH + 0.16c^{o_2} - 0.0058c^{o_2^2}) \rho^{cell} \frac{c_g}{c_g + k_m^l} \quad (8)$$

$$Q^{glucose} = -0.5Q^{lactate} \quad (9)$$

$$pH = -0.1c^{lactate} + 7.5 \quad (10)$$

where $V'_{\max}$ is the maximum consumption rate of oxygen, K'_m is the Michaelis–Menten constant for oxygen, k_m^l is the Michaelis–Menten constant for lactate, and ρ^{cell} is the cell density. More details of the theoretical formulation can be found in our previous studies (Gu et al., 1998, 1999a; Gu and Yao, 2003; Gu et al., 2004; Huang and Gu, 2008; Jackson et al., 2011a; Yao and Gu, 2007).

2.1. Constitutive model for cell density

In this study, a new theoretical formulation for rate of cell density change has been developed based on previous theoretical framework on microbial cell growth (Lin et al., 2000):

$$\frac{\partial \rho^{cell}}{\partial t} = \zeta \times \rho^{cell} \quad (11)$$

where ρ^{cell} is the cell density, and ζ is essentially the rate of normalized cell density change. We propose that the rate ζ of cell density change in the IVD tissue in general depends on the glucose concentration as follows:

$$\zeta = \alpha \cdot \left(\frac{c_g - c_{g0}}{c_g + k_1} - \frac{|c_g - c_{g0}|}{c_g + k_2} \right) \quad (12)$$

where c_g is the glucose concentration (in mM), c_{g0} is the threshold glucose concentration necessary for IVD cell survival; below which cells begin to die. The positive parameters α , k_1 and k_2 are determined by the biology of IVD cells.

Previous experimental studies have shown that IVD cell death is initiated when glucose levels fall below 0.5 mM, and at 0.2 mM all cells die in 3 days (Bibby et al., 2002; Bibby and Urban, 2004; Horner and Urban, 2001). Based on these studies and the assumption that cell density does not change for glucose concentration values above 0.5 mM, we have that $c_{g0} = 0.5$ mM, $k_1 = k_2 = 0.2$ mM and $\alpha = 1 \text{ day}^{-1}$. So Eq. (12) becomes (see Fig. 1a)

$$\zeta = \alpha \cdot \left(\frac{c_g - 0.5}{c_g + 0.2} - \frac{|c_g - 0.5|}{c_g + 0.2} \right) \quad (13)$$

When the glucose concentration is constant, the rate of change in cell density is constant. Under this special condition, it follows from Eqs. (11) and (13) that

$$\rho^{cell} = \rho_0^{cell} e^{\int_0^t \zeta dt} = \rho_0^{cell} e^{\alpha \left(\frac{c_g - 0.5}{c_g + 0.2} - \frac{|c_g - 0.5|}{c_g + 0.2} \right) t} \quad (14)$$

where ρ_0^{cell} is the initial cell density. Eq. (14) shows that cell density declines exponentially with time when glucose concentration (c_{g0}) is below threshold (Fig. 1b).

3. Finite element analysis

A realistic, three-dimensional IVD geometry was generated based on an L2-L3 human disc (41 years old, male, healthy), see Fig. 2a. The IVD was modeled with three distinct regions: nucleus pulposus (NP), annulus fibrosus (AF), and cartilaginous endplate (CEP). Because of symmetry, only the upper right quarter of IVD (Fig. 2b) was modeled and meshed with 13,981 quadratic Lagrange tetrahedral elements (Fig. 2d) using COMSOL software (COMSOL 4.2a, COMSOL, Inc., Burlington, MA). The convergence criterion was the relative error tolerance less than 10^{-6} . In the model, the fixed charge density, hydraulic permeability, and solute diffusivities are functions of water content (i.e., porosity) which depends on the deformation of the IVD (Gu et al., 2003, 2004; Yao and Gu, 2004). The weak form of FEM formulation was based on the work by Sun et al. (1999).

Both non-degenerated and degenerated IVD tissues were analyzed. The material properties used were based on experiments from literature (Gu et al., 1999b, 2004; Gu and Yao, 2003; Iatridis et al., 1997; Maroudas, 1975; Maroudas et al., 1975; Roberts et al., 1989; Setton et al., 1993; Yao and Gu, 2007), details are listed in Table 1. To simulate the degenerated IVD, the tissue was modeled with reduced disc height (An et al., 2005), hindered CEP permeability (Bernick and Cailliet, 1982; Nachemson et al., 1970; Nguyen-minh et al., 1998; Urban et al., 2001), lower water content and smaller fixed charge density (Antoniou et al., 1996; Buckwalter et al., 1985; Gruber and Hanley, 1998; Roberts et al., 1989; Sztrolovics et al., 1999), and stiffer mechanical properties (Iatridis et al., 1999), as compared with non-degenerated IVDs, see Table 1. Boundary and initial conditions are listed in Table 2.

The deprivation of nutrition supply at blood source was simulated by reduction in nutrition level at CEP and AF boundaries. The effects of 100%, 75%, 60%, 50% and 30% of normal nutrition level at both CEP and AF boundaries on cell viability were simulated. In these simulations, both non-degenerated and degenerated IVDs were first equilibrated with normal nutrition boundary and initial conditions (as listed in Table 2) for 10 days, followed by a reduction of nutrition level at the boundary for another 10 days.

Effects of mechanical compressions on cell viability were modeled as follows: the tissue was initially equilibrated with aforementioned initial and boundary conditions for a period of t_1 ($t_1=10$ days), followed by a ramp compression [10% axial compression within a period of t_2 ($t_2=1$ h)]. After stress relaxation for a period of t_3 ($t_3=5$ days) at this new configuration, for dynamic compression cases, axial sinusoidal compression was applied to the tissue for another 5 days, see Fig. 2c. For static compression cases, displacement was maintained at u_0 for another 5 days after t_3 .

In addition, the effect of glucose threshold value (c_{g0}) on cell viability was also investigated with non-degenerated IVDs. Three different threshold values (i.e., $c_{g0} = 0.7$ mM, 0.5 mM and 0.3 mM) were used in the simulations. In these simulations, the disc was equilibrated with 50% of normal nutrition level at boundaries for 10 days at each threshold value.

4. Results

The mechanical signals (stress, strain, fluid pressure, fluid flux, etc.), chemical signals (sodium and chloride ion concentrations, oxygen, glucose, and lactate concentrations, and pH value), electrical signals, and cell density distributions within the IVD were calculated.

Because of page limitation, only results relevant to cell density (normalized by its initial value in each region) and glucose level were reported.

4.1. Effect of reduction of nutrition level at IVD boundaries on cell density

Our results showed that cell density decreased substantially with reduction of nutrition level at boundaries in non-degenerated discs (Fig. 3). Cell death was initiated primarily near the NP–AF interface on the mid-plane (Fig. 3b). The NP region was more severely affected, compared with AF region (Fig. 3c). This effect of reduction of nutrition level on the cell density was more pronounced in degenerated IVDs. After 10 days of nutrition reduction (50%), the minimum glucose concentration in degenerated disc was slightly lower than that in non-degenerated disc (Fig. 4a) but the difference in minimum cell density (normalized) between degenerated and non-degenerated discs was significant (Fig. 4b). Note that the minimum cell density decreased monotonically with time even though the minimum glucose concentration recovered in IVDs (Fig. 4).

4.2. Effect of dynamic compression on cell density

Dynamic compressions with different combinations of magnitude u ($u=10\pm2.5\%$, $\pm5\%$) and frequency f ($f=1, 10, 20$ cycle/day) were simulated. It was found that dynamic compressions did not affect the cell density in non-degenerated IVDs, compared with the static case, because the glucose levels in non-degenerated IVDs did not fall below the threshold value (i.e., 0.5 mM) for cell survival (data not shown). The cell density in the degenerated disc with dynamic compression was higher compared with that of static compression (Fig. 5). For example, the minimum value of normalized cell density was 0.37 in disc with static compression (Fig. 5a), compared to the value of 0.62 in the same disc with dynamic compression ($10\pm2.5\%$, 20 cycle/day), see Fig. 5d. The degree of improvement in cell viability in degenerated discs depended on both loading frequency and amplitude (Fig. 5).

4.3. Effect of variation of threshold values on cell density

Our results showed that an increase in the threshold value led to higher values in minimum glucose concentration (Fig. 6a), but lower values in minimum cell density (Fig. 6b). In addition, the increase in threshold value caused earlier initiation of cell death (Fig. 6b). The cell death initiated near the NP–AF region and spread towards the NP region for all cases simulated (data not shown).

5. Discussion

In this study, the effects of reduction of nutrition levels at boundaries, degeneration, and dynamic compression on cell viability in IVDs in a time-dependent manner were investigated. To this end, a novel constitutive model for cell viability was developed based on the experimental data (Bibby et al., 2002; Bibby and Urban, 2004; Horner and Urban, 2001), and incorporated into the mechano-electrochemical mixture theory to regulate the cell density.

This new constitutive model can more realistically predict cell viability in IVD, without the peculiar phenomenon of resurrection of dead cells when glucose level recovers (see Figs. 4 and 6). For the case where a degenerated IVD is statically compressed by 10% (Jackson et al., 2011a), our current model predicts that at steady state, the minimum glucose concentration in disc is 0.495 mM and the minimum cell density is 0.0, compared to the predicted values of 0.292 mM for minimum glucose concentration and 0.309 for normalized minimum cell density in the same IVD using the previous model for cell viability (Jackson et al., 2011a; Shirazi-Adl et al., 2010). In addition, our calculation shows that the affected

volume (defined as the domain where more than 5% of cells die) is only 2.67% of the total volume (NP, AF and CEP) of IVD predicted by our model, compared to the value of 34.19% predicted by the previous cell viability model (in which resurrection of dead cells would occur). This is because in the previous model for cell viability, the cell density was assumed to be linearly related to the glucose concentration (in the range of 0.2 mM to 0.5 mM) (Shirazi-Adl et al., 2010). However, in reality, when the glucose concentration is lower than the threshold value (i.e., 0.5 mM), the cell density would continue to decline until the glucose concentration recovers to the threshold value, or cell density would reach to zero. Our current model can correctly predict this phenomenon (also see Figs. 4 and 6). These comparisons also indicate that predicted results are sensitive to the choice of the constitutive models for cell viability; thus, it is important to have a more realistic constitutive model for cell viability in order to investigate the mechanobiology of IVD numerically.

Perturbations in nutrition supply at boundaries because of aging, blood aneurysms or smoking (Frymoyer et al., 1983; Gynzelbe, 1974; Holm and Nachemson, 1988) could all adversely influence the activities and viability of disc cells, and resultantly, disc function. Our results demonstrate that as the nutrition level at boundaries falls below ~60% of normal value, cell death begins to initiate near the NP–AF interface on the mid-plane and spread toward the inner NP region. When the nutrition concentration on the disc edge drops below ~30% of normal level, most of the cells on the mid-plane of the NP region will die in non-degenerated IVDs (Fig. 3). For the degenerated case, the drop in nutrition levels at the tissue boundary caused larger magnitudes of cell death (compared to the non-degenerated case). This may be because reduced diffusivity and permeability due to lower water content decreases the nutrients transport through the CEP to NP cells, which consequently reduces the nutrients distribution around the cells.

The finding that dynamic compression improves cell viability is mainly due to the fact that dynamic compressions increase the diffusivities of nutrient (Fig. 7a and b), and improve the concentration of cell nutrition (Fig. 7c and d), which aid in maintaining cell metabolism and viability. This will, consequently, promote synthesis and maintenance of the matrix, which will in turn prevent or reduce the degeneration of the IVD. Our findings are in agreement with reports from the literature (Iatridis et al., 2009; Kasra et al., 2003; Kroeber et al., 2005; Wang et al., 2007; Wuertz et al., 2009). Since dynamic compression is a more typical mechanical loading regimen for the human intervertebral discs (as compared with static compressions), our results under dynamic loads are indicative of real time compression effects on nutrition transport and cell viability in the human IVD.

As expected, variation of the threshold values influences the magnitude and initiation time of cell death (Fig. 6). The larger the threshold value is, the earlier the cell death initiates, and the more cells die (Fig. 6b). The effect of variation of threshold value on glucose concentration change was opposite to that on cell density change. The larger the threshold value, the higher the glucose level remained in the IVD (Fig. 6a). This is because larger threshold value causes more cell death, leading to smaller consumption of glucose and consequently, resulting in more accumulation of glucose in the IVD.

Our findings on the location (i.e., near NP–AF interface) of cell death initiation differs from the previous study by Shirazi-Adl et al. (2010), which found that the initiation of cell death was located in the center of the NP region. This may be due to different material properties and different cell density models used. However, our finding is in agreement with results of literature (Walsh and Lotz, 2004), which found that cells at the NP–AF interface (i.e., outer NP cells, inner and middle AF cells) were more affected than the other parts by dynamic loadings.

One limitation of this study was that only glucose has been considered in our cell viability model. Even though it has been reported that inclusion of pH did not significantly influence cell viability [compared with the consideration of glucose alone in the cell viability model (Shirazi-Adl et al., 2010)], future works are necessary to explicitly incorporate pH factor into our cell viability model to more accurately investigate and predict the cell viabilities and functions in the IVD. Another limitation was that the anisotropic properties of the AF were not taken into consideration in this study. This will be included in our future studies.

In summary, this work numerically analyzed the effects of reduction of nutrition levels at boundaries, degeneration, and dynamic compression on cell viability in a realistic, three-dimensional intervertebral disc in a time-dependent manner. A new constitutive model for cell viability has been developed based on experimental data. This model is capable of predicting cell density distributions as well as both the region and time at which cells start to die within the intervertebral disc under different biological and physical conditions. The present numerical simulation is a valuable supplement to experimental studies of cell viability and transport of nutrients in avascular, hydrated, cartilaginous tissues under nutrition deprivation, degeneration, and mechanical loading conditions. The model could be used not only to delineate biomechanical etiology of disc degeneration, but also to provide guidance for the treatment of disc degeneration in physical therapy.

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Fig. 1.

(a) The rate of cell density (normalized) change as a function of glucose concentration; (b) changes in cell density (normalized) with time at several constant glucose levels. Cells begin to die when glucose levels fall below 0.5 mM, and cell density approaches zero when the glucose concentration is lower than 0.2 mM for a period of 3 days (Bibby and Urban, 2004). No change in cell density occurs when the glucose concentration is above 0.5 mM.

Fig. 2.

(a) Picture of the 3D intervertebral disc; (b) schematic of the upper right quarter used in our finite element model; (c) the time history of the displacement (u_0) boundary condition at the surface of the IVD with dynamic compression and (d) mesh of the 3D intervertebral disc.

Fig. 3.

Effects of reduction of nutrition level at boundaries on cell density in non-degenerated IVDs at the end of a 10-day period—cell density distribution with (a) normal (i.e., 100%) nutrition level (minimum:1.00); (b) 50% of normal level (minimum:0.11) and (c) 30% of normal level (minimum:0.02). The cell density was normalized by its initial value in each region (see Table 1).

Fig. 4.

The effect of degeneration on the cell density and glucose concentration in the IVDs with 50% of normal nutrition level at the end of a 10-day period. Comparison of: (a) minimum glucose concentration and (b) minimum cell density (normalized) in non-degenerated and degenerated discs.

Fig. 5. Effects of dynamic compression on cell density (normalized) distribution in degenerated IVD: (a) 10% static compression, minimum—0.37; (b) dynamic compression ($10\% \pm 2.5\%$, 1 cycle/day), minimum—0.45; (c) dynamic compression ($10\% \pm 5.0\%$, 1 cycle/day), minimum—0.59 and (d) dynamic compression ($10\% \pm 2.5\%$, 20 cycle/day), minimum—0.62.

Fig. 6. Variation of threshold values for the minimum glucose concentration and minimum cell density (normalized) in the non-degenerated IVDs with 50% of normal nutrition level at boundary: (a) time response of the minimum glucose changes and (b) time response of the minimum normalized cell density.

Fig. 7. Effects of dynamic compression on averaged diffusivity of glucose changes with time in the (a) NP region and (b) AF region and on averaged glucose concentration changes with time in the (c) NP region and (d) AF region in the degenerated IVDs.

Table 1

Material properties of the IVD used in finite element analysis.

IVD properties	Regions	Non-degenerated	Degenerated
Reference water content ϕ_0^w ^a	AF	0.75	0.68
	NP	0.86	0.78
	CEP	0.60	0.3
Thickness (mm)	AF	10	9
	NP	10	9
	CEP	0.6	0.6
ρ_0^{cell} (cells/mm ³) ^b	AF	9000	
	NP	4000	
	CEP	15,000	
c^F (mol/m ³) ^c	AF	150	125
	NP	250	175
	CEP	90	90
Parameters for diffusivity ^d $\frac{D^\alpha}{D_0^\alpha} = \exp \left[-A \left(\frac{r_\alpha}{\sqrt{k}} \right)^B \right]$	AF	$A = 1:29 \ B = 0:372$	
	NP	$A = 1:25 \ B = 0:681$	
	CEP	$A = 1:29 \ B = 0:372$	
	AF	$a = 0:00044 \text{ nm}^2 \ n = 7:193$	
Parameters for permeability ^e $k = a \left(\frac{\phi^w}{1 - \phi^w} \right)^n$	NP	$a = 0:00339 \text{ nm}^2 \ n = 3:240$	
	CEP ^f	$a = 0:0248 \text{ nm}^2 \ n = 2:154$	
	AF		
Elasticity constants ^g	AF	$\lambda = 300 \text{ kPa}$	$\lambda = 700 \text{ kPa}$
		$\mu = 100 \text{ kPa}$	$\mu = 150 \text{ kPa}$
	NP	$\lambda = 15:6 \text{ kPa}$	$\lambda = 25:8 \text{ kPa}$
		$\mu = 0:18 \text{ kPa}$	$\mu = 0:61 \text{ kPa}$
	CEP	$\lambda = 100 \text{ kPa}$	$\lambda = 100 \text{ kPa}$
		$\mu = 200 \text{ kPa}$	$\mu = 200 \text{ kPa}$

^aCalculated from results in Antoniou et al. (1996) and Magnier et al. (2009).^bFrom Maroudas et al. (1975).^cCalculated from results in Antoniou et al. (1996) and Jackson et al. (2011a).^dFrom Gu et al. (2004).^eFrom Gu et al. (2003).^fFrom Jackson et al. (2011a).^gFrom Iatridis et al. (1999), Iatridis et al. (1997), Jackson et al. (2011a) and Johannessen and Elliott (2005).

Table 2

Boundary and initial conditions of the IVD used in finite element analysis.

Boundary conditions		Initial conditions		
		NP	AF	CEP
AF peripheral	$c^{glucose} = 5 \text{ mM}$			
	$c^{O_2} = 5.8 \text{ kPa}$	$u = 0$		
	$c^{lactate} = 0.9 \text{ mM}$	$v = 0$		
	$c^{Na^+} = c^{Cl^-} = 0.15 \text{ M}$	$w = 0$		
CEP top	$\sigma_{xx} = \sigma_{xz} = \sigma_{xy} = 0$	$c^{glucose} = 4 \text{ mM}$		
	$c^{glucose} = 4 \text{ mM}$	$c^{O_2} = 5.1 \text{ kPa}$		
	$c^{O_2} = 5.1 \text{ kPa}$	$c^{lactate} = 0 \text{ mM}$		
	$c^{lactate} = 0.8 \text{ mM}$	$c^{Na^+} = c^{Cl^-} = 0.15 \text{ M}$		
	$c^{lactate} = 0 \text{ mM}$			
	$c^{Na^+} = c^{Cl^-} = 0.15 \text{ M}$			
	$u_z = 0$ for no compression			
	$u_z = 0$ for compression			
Mid-plane ($z=0$)	$\sigma_{zx} = \sigma_{zy} = 0$			
	$j_z^{water} = j_z^{glucose} = j_z^{O_2} = j_z^{lactate} = j_z^{Na^+} = j_z^{Cl^-} = 0, u_z = 0, \sigma_{zx} = \sigma_{zy} = 0$			
Plane ($x=0$)	$j_z^{water} = j_z^{glucose} = j_z^{O_2} = j_z^{lactate} = j_z^{Na^+} = j_z^{Cl^-} = 0, u_x = 0, \sigma_{xy} = \sigma_{xz} = 0$			