**Electronic Supplementary material**

For “*Injury-related cell death and proteoglycan loss in articular cartilage: Numerical model combining necrosis, reactive oxygen species, and inflammatory cytokines*” (in *PLOS Computational Biology*) by

Joonas P. Kosonen1, Atte S.A. Eskelinen1, Gustavo A. Orozco1,2, Petteri Nieminen3, Donald D. Anderson4, Alan J. Grodzinsky5, Rami K. Korhonen1, and Petri Tanska1

1*Department of Technical Physics, University of Eastern Finland, Kuopio, Finland*

*2Department of Biomedical Engineering, Lund University, Lund, Sweden*

*3Institute of Biomedicine, University of Eastern Finland, Kuopio, Finland,*

*4Departments of Orthopedics & Rehabilitation and Biomedical Engineering, University of Iowa, Iowa City, IA, USA*

5*Departments of Biological Engineering, Electrical Engineering and Computer Science and Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, MA, USA*

**Corresponding author:**

\*Joonas P. Kosonen

Department of Applied Physics

University of Eastern Finland

Yliopistonranta 1 F

POB 1627, Kuopio FI-70211, Finland

Tel: +358 50 3043474

joonas.kosonen@uef.fi

**S1 Text. Biomechanical material model**

Cartilage was modeled as a fibril-reinforced porohyperelastic material model with Donnan osmotic swelling and chemical expansion (FRPHES). Previously, the FRPHES material model has been successfully used to simulate the experimentally observed cartilage behavior after biomechanical compression [1–4]. In this material model, the cartilage is considered as an anisotropic biphasic material including a solid phase with fibrillar (collagen) and non-fibrillar (proteoglycans, PG) components and a fluid phase. Furthermore, the material model considers depth-dependent PG (fixed charge density, FCD) and water content as well as depth-wise collagen distribution and orientation (see S1 Table) [1,3].

Cauchy stress tensor of a Neo-Hookean solid material was used to describe stresses in the non-fibrillar solid matrix [3,5]:

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|  |  | (S1) |

where is the deformation gradient tensor, is the unit tensor and is the volumetric deformation, i.e., determinant of the deformation gradient tensor. The bulk and shear moduli of the non-fibrillar matrix were determined as

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| --- | --- | --- |
|  |  | (S2) |
|  |  | (S3) |

where (0.16 MPa [1]) is the elastic modulus and the Poisson’s ratio of the solid non-fibrillar matrix (0.42 [6]).

In the current material model, stress tensor of the fibrillar collagen network arises from the sum of the collagen fiber stresses in each point, including stresses in primary and secondary fibrils [3]. Hence, collagen network stress tensor was defined as

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|  |  | (S4) |

where the is the Cauchy stress tensor of the collagen fiber *k* and *totf =* 9 [3] refers to the total number of fibers. Collagen fiber architecture was modeled as observed in young bovine cartilage (50° in the deep zone, 10° in the superficial zone [90° = perpendicular to the surface]) [1]. For each fibril (primary fibril = p, secondary fibril = s), the Cauchy stress tensor was defined as [3,4]:

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|  |  | (S5) |

where is the depth-dependent relative collagen density (see S1 Table ), *C* is the ratio between primary and secondary fibril densities (3.009 [3]), is the normalized unit vector for fibril orientation [3] and is the outer product operation. Stress in the collagen fibrils (scalar) was defined as

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|  |  | (S6) |

where is the initial constant elastic modulus of a single collagen fiber (20 MPa [1]) and is the logarithmic fibril strain [4].

Fluid flow in the non-fibrillar porous matrix was modeled via Darcy’s law

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|  |  | (S7) |

where is the flow flux in the non-fibrillar matrix, is the hydraulic permeability ( [1]), and is the pressure gradient in the cartilage.

The chemical expansion stress caused by repulsion of the negative charge groups in PGs was modeled as

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|  |  | (S8) |

where and are material constants [3], and are external and internal activity coefficients [7], and is the mobile anion concentration in the cartilage [3,8]. The depth-dependent FCD concentration is described as a function of volumetric deformation

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|  |  | (S9) |

where is the initial depth-wise FCD and is the porosity, i.e., fluid volume fraction, both presented in S1 Table.

Donnan osmotic swelling in equilibrium after initial swelling was modeled as

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|  |  | (S10) |

where and are external and internal osmotic coefficients [7], is the external salt concentration (0.15 M), is the molar gas constant (8.3145 J/mol K) and is the absolute temperature (293 K).

Finally, the total stress tensor of the cartilage tissue was determined as

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| --- | --- | --- |
|  |  | (S11) |

where is the chemical potential of water [5].

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