NUMERICAL SIMULATION OF HYDROGELS FOR CARTILAGE TISSUE ENGINEERING USING OPEN-SOURCE SOFTWARE

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Abstract

Articular hyaline cartilage covers articulating bone surfaces in diarthroidal joints of the human body. Despite the availability of palliative and surgical treatment options, they cannot fully regenerate damaged tissue at a defect site. Cartilage tissue engineering using electrical stimulation of hydrogel samples has been proven to be an effective strategy. The current study deals with a simulation model of electrosensitive hydrogels for cartilage tissue engineering. The simulations are performed using the open-source high-performance finite element software NGSolve. The aim is to analyse different quantities, including ionic concentrations, electric potential, and electric conductivity in a hydrogel sample and the surrounding medium.

1 Introduction

Articular cartilage is an elastic and translucent connective tissue mainly composed of water, chondrocytes and extracellular matrix [1]. It has a limited natural healing and regenerating ability because it is void of blood, lymphatic vessels, and nerves. Hydrogels have remarkable potential in cartilage regeneration as they provide a three-dimensional environment suitable for the growth of chondrocytes [2]. Hydrogel scaffolds preserve the morphology and phenotype of chondrocytes, which can be further enhanced by applying suitable biophysical stimuli such as electrical stimulation [2]. These scaffolds can then be implanted at the defect site, as illustrated in Fig. 1. Electrical stimulation can lead to the activation of ion channels and proteins. It alters the ionic concentrations, activating gene expression, mobilising growth and transcription factors, and promoting cell adhesion [1]. Numerical simulations can be utilised to gain insight into these mechanisms across a range of length scales.

2 Mathematical model

Computational modelling and simulation techniques complement experimental studies, offering predictive insights, guiding experimental design, and enabling the exploration of scenarios that may be difficult or impossible to achieve experimentally. Several modelling theories exist in the literature that can be used to model the electrical stimulation of electrosensitive hydrogels. Most of these theories comprise nonlinear Poisson-Nernst-Planck (PNP) equations, written as follows:

$$\nabla^2\psi + \frac{F}{\varepsilon_o\varepsilon_r}\left(\sum_{k=1}^{n} z^k c^k + z^f c^f\right) = 0$$

$$D_k\nabla^2 c^k + D_k\frac{z^k F}{RT}\nabla(c^k\nabla\psi) = 0$$

where ε_r is the medium's relative permittivity, ε_o is the dielectric constant, ψ is the electric potential, F is Faraday's constant and $c^{k,f}$ are the ionic concentrations

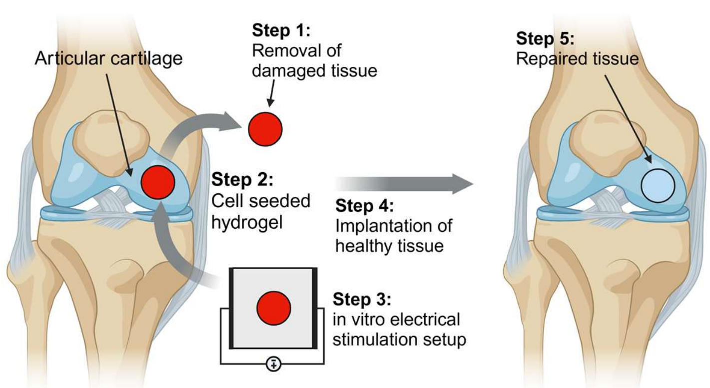

Figure 1. Different steps involved in articular cartilage tissue engineering using electrical stimulation (Created in Biorender).

having valence $z^{k,f}$. Moreover, D^k is the diffusivity of ions, T is temperature, and R is the gas constant. We have utilised the transport model proposed by Wallmersperger et al. [3] for the finite element simulations as it has a reduced number of unknowns. The PNP equation is solved numerically using the open-source numerical software NGSolve [4] for electrosensitive hydrogels for cartilage tissue engineering. Previously, we have presented a similar numerical simulation model for cartilage tissue engineering [5] using the finite element software FEniCS [6]. Compared to FEniCS, NGSolve is preferred due to its integrated CAD kernel and Netgen mesh generator, reduced dependencies, and increased user-friendliness.

First, validation of the proposed finite element model was done. Figures 2 and 3 show representative one- and two-dimensional results for the concentration of anions, which agree with the results given in [3].

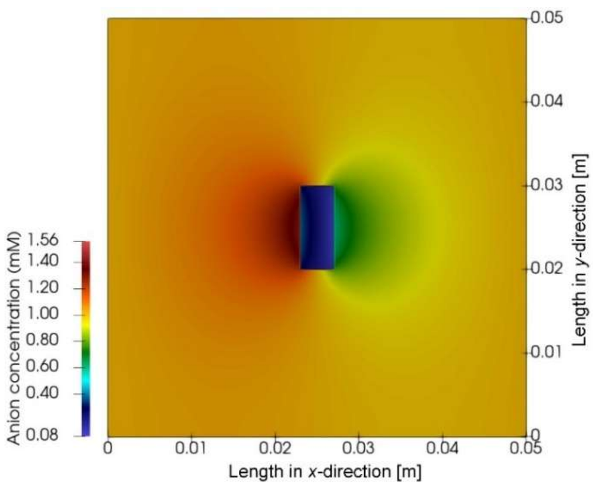

Figure 2. Two-dimensional anion concentration profile for a hydrogel scaffold immersed in a solution.

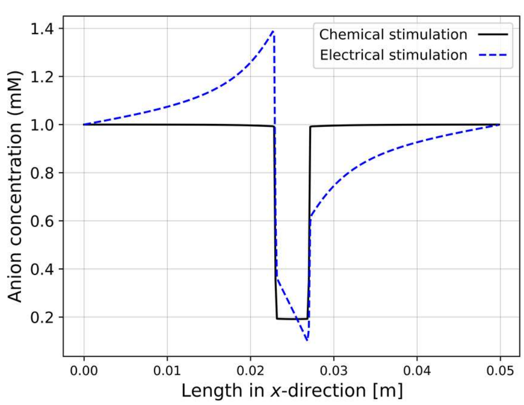

Figure 3. Comparison of one-dimensional anion concentration profile under chemical and electrical stimulation.

Following the validation, the model was extended for a two-dimensional circular hydrogel specimen immersed in solution as used in cartilage tissue engineering [5]. These simulation studies help to make a rational selection of experimental parameters. A representative graph of the electric conductivity is illustrated in Fig. 4.

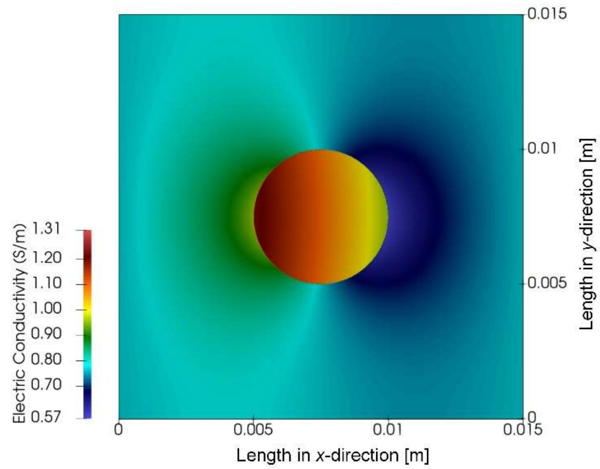

Figure 4. Electrical conductivity profile for a circular hydrogel scaffold in the electrolyte solution under an external electric field.

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