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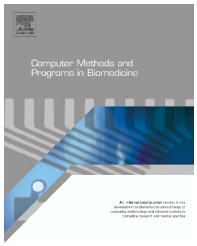

Computational analysis of cartilage implants based on an interpenetrated polymer network for tissue repairing

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ABSTRACT

Interpenetrated polymer networks (IPNs), composed by two independent polymeric networks that spatially interpenetrate, are considered as valuable systems to control permeability and mechanical properties of hydrogels for biomedical applications. Specifically, poly(ethyl acrylate) (PEA)–poly(2-hydroxyethyl acrylate) (PHEA) IPNs have been explored as good hydrogels for mimicking articular cartilage. These lattices are proposed as matrix implants in cartilage damaged areas to avoid the discontinuity in flow uptake preventing its deterioration. The permeability of these implants is a key parameter that influences their success, by affecting oxygen and nutrient transport and removing cellular waste products to healthy cartilage. Experimental try-and-error approaches are mostly used to optimize the composition of such structures. However, computational simulation may offer a more exhaustive tool to test and screen out biomaterials mimicking cartilage, avoiding expensive and time-consuming experimental tests. An accurate and efficient prediction of material's permeability and internal directionality and magnitude of the fluid flow could be highly useful when optimizing biomaterials design processes. Here we present a 3D computational model based on Sussman–Bathe hyperelastic material behaviour. A fluid structure analysis is performed with ADINA software, considering these materials as two phases composites where the solid part is saturated by the fluid. The model is able to simulate the behaviour of three non-biodegradable hydrogel compositions, where percentages of PEA and PHEA are varied. Specifically, the aim of this study is (i) to verify the validity of the Sussman–Bathe material model to simulate the response of the PEA–PHEA biomaterials; (ii) to predict the fluid flux and the permeability of the proposed IPN hydrogels and (iii) to study the material

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domains where the passage of nutrients and cellular waste products is reduced leading to an inadequate flux distribution in healthy cartilage tissue. The obtained results show how the model predicts the permeability of the PEA–PHEA hydrogels and simulates the internal behaviour of the samples and shows the distribution and quantification of fluid flux.

1. Introduction

Articular cartilage defects are a common type of injury in aged population [1]. Most common treatments consist of removing the diseased and undermined cartilage to stop inflammation and pain, including chondrectomy and debridement [2]. In both cases, the empty area is covered with a fibrous self-regenerated tissue with similar structure to healthy tissue but with poor mechanical properties [3]. Fibered matrix implants are explored as a substitution of damaged tissue providing good mechanical properties, mimicking cartilage microstructure [4], avoiding discontinuity in flow uptake with healthy tissue (host tissue) which prevent its deterioration (Fig. 1). Recently, these lattices are also proposed as *ex vivo* platforms in bioreactors to test scaffolds for cartilage tissue engineering to mimic the host healthy tissue *in vivo*. They act *in vitro* as support systems to lodge scaffolds and maintain the correct fluid flow [5].

In this sense, the internal structure of the fibered matrix implant is a major biomaterial characteristic for tissue engineering [6,7] that provide structural support for mechanical loads and keep the adequate distribution of stress within the tissue. Such constructs offer a flexible physical environment to allow passage of nutrients and removing cellular waste products contained in the synovial fluid in response to dynamic compression process similar to those observed in physiological tissue conditions [8]. Cells nutrition and by-product exchange are diffusive mediated processes occurring in the cellular surrounding region [9]. Therefore, these events are of special interest in biomedical implants for cartilage as being the only mean of nutrient uptake by chondrocytes, due to the avascular and no neural nature of this tissue [10].

The intrinsic permeability coefficient of the implant materials and inner fluid flux analysis are determinant to ensure homogeneous supply of nutrients thorough the system [11]. In this sense, the inner flux analysis provides insight into the adequate nutrient distribution within the healthy tissue [12]. To experimentally control both parameters, numerous manufacturing techniques have been developed, from particulate-leaching techniques, where salt, wax or sugar porogens are used to create the pores or channels [13], to the "rapid prototyping" where the fabrication process is computationally controlled [14]. Most of these methods can rapidly produce fibered matrix implants; however, the critical variables such as porosity, mechanical properties and diffusive parameters are not controlled.

The observed shortcomings are partially overcome by the use of interpenetrated polymer networks (IPNs) [15]. IPNs are polymeric systems of two or more independent networks which are spatially interlaced, but do not have covalent bonds between them (Fig. 2). The resulting biomaterial offers not only good mechanical properties and permeability but also high thermo stability and good dielectric properties [16].

Despite of the above mentioned advances in mimicking the natural tissue environment, oversimplified biomaterials for cartilage tissue regeneration are still being used [17]; since high experimental costs and consumed manufacturing time make inefficient the optimization process to obtain custom adequate biomaterials to host tissue singularities [18].

These observations motivate the development of new computational models to simulate the behaviour of each specific biomaterial avoiding try-and-error experimental assays and also providing additional insights in IPN manufacturing processes [19]. Due to the wide variety of hydrogel compositions and manufacturing procedures [20], experimental assays to characterize their behaviour are costly and time-consuming.

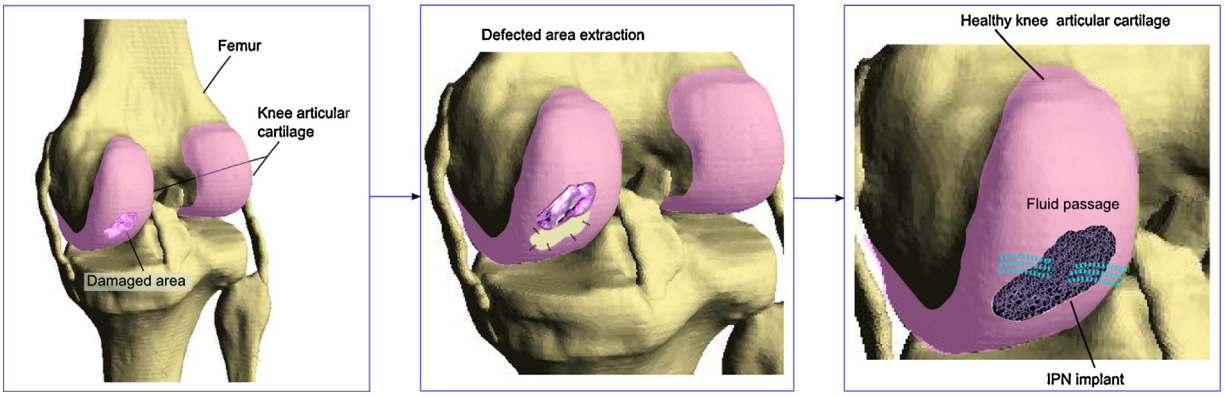

Fig. 1 – Schematic representation of IPN implant process in removed damage areas of knee cartilage. Implant prevents interruption of the flow passage that carries nutrients and cellular waste products.