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Published in:
Journal of Physics: Conference Series

DOI:
10.1088/1742-6596/633/1/012134

Published: 21/09/2015

Document Version
Publisher's PDF, also known as Version of record

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Please cite the original version:
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To cite this article: Y Bilotsky and M Gasik 2015 J. Phys.: Conf. Ser. 633 012134

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Modelling of poro-visco-elastic biological systems

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Abstract. The research of mechanical properties of poro-visco-elastic biomaterials is an important task, especially for tailoring the best conditions for in-growth and healing of implants. In this work we analysed the behaviour of biomaterials under different static and dynamic loading regimes, in "dry" and "wet" conditions. Retrieved data revealed nonlinear relations between applied force and resulting deformation, with time and frequency dependence. These features were described by a nonlinear model, which reasonably fits mentioned peculiarities. The simplified model was validated with numerical simulations using COMSOL software. Upon validation it allows incorporation of the experimental data obtained by biomechanical spectroscopy towards prediction of biomaterials behaviour in "in vitro" conditions, with the purpose to extrapolate to clinically-relevant environment.

1. Introduction
Investigation of mechanical properties of biological systems is very complicated objective and requires specific knowledge of every part of this system and creation a general model is a problematic task [1,2]. Even in the case of biomechanical behavior of the natural (bone, cartilage) or artificial (relevant implants), without inclusion of cellular signals, biochemical pathways and external environment, it is very difficult to obtain an engineering model capable of prediction of the poro-visco-elastic behavior of such materials, needed for their proper design.

It is known that biomechanical properties are critical for biological processes, and these properties are regulating the signals sent to the cells [3]. Due to variety of parameters involved and the obvious limitations of in vivo studies, computational mechanobiology is often applied to determine the quantitative rules that govern the effects of mechanical loading on tissue differentiation, growth, adaptation and maintenance by trial-and-error. From a mechanics point of view, the task is considered a ‘boundary value problem’, whereby the boundary loads of a domain are translated into local mechanical variables within the domain, depending on the geometry and mechanical properties of its materials [1-3]. Such problems are usually solved with finite element analysis (FEA).

Whereas numerous studies were performed in this area and their results were sometimes correlated with in vivo experiments, the feedback did not allow deployment of a reverse design scheme, which would be capable to tell the desired properties of the scaffold or implant for specific application and patient. In the most cases, this is limited to purely geometrical constrains (whether implant fits the site and how well) or mechanical criteria (maximal expected stress vs. body weight, expected local stresses concentrators or fatigue life).

In this work we attempt to derive simplified yet practical model of characterization of porous scaffolds intended for articular cartilage (AC) correction surgery. The structure, functions and
behavior of AC are very complex and highly anisotropic [4]. Articular cartilage is a living material composed of a relatively small number of cells known as chondrocytes surrounded by a multicomponent matrix. Mechanically, AC (Figure 1) is a composite with widely differing properties, of which weight 70 to 85% is water. The remainder of the tissue is composed primarily of proteoglycans (protein core to which glycosaminoglycans are attached to form a bottlebrush-like structure) and collagen II [4,5]. These proteoglycans can bind or aggregate to a backbone of hyaluronic acid (HA) to form a macromolecule with a weight up to 200 million [5]. Approximately 30% of the dry AC weight is composed of proteoglycans, which concentration and water content vary through the depth of the tissue.

![Figure 1. The structure of the knee joint. Articular cartilage is shown in light color.](image)

Synthetic materials with fibrous origin are often used for AC correction applications. There 75-85% porous scaffolds are usually attached to the bony side of the cartilage, leaving other side to exposure to synovial fluid with HA. In this work the target was to find the proper simple model which can describe the poro-visco-elastic biomaterials for easier use in clinical practice, such as to find answers which scaffold design would be the most appropriate for specific patient conditions.

2. Models for porous scaffolds.

There are many simple and more complex expressions for porous materials intended for AC applications. Mechanically the description of these materials might be divided into two categories, called here respectively "dry" and "wet" conditions. In the first case, the material is analyzed without liquid, assuming complete drained conditions and neglecting the gas (air) viscosity and compressibility in the pores. This is justified for low loading frequencies, but as most of the physiological frequencies fit within 1 Hz region, dry conditions might be seen as relevant for the porous skeleton analysis. In the wet case, the material is fully saturated with a fluid (can be Newtonian or non-Newtonian) and the analysis can be performed for two categories: drained (free fluid in and out flow) and undrained (fluid flow constrained). Here we are limiting analysis only for drained conditions, as supported by our experiments.

Besides mechanical characterization (e.g. simple compression tests), the model sought is required to provide consistent answers for two important modes, namely creep at constant load and frequency response under oscillating dynamic load. These modes are combined in nature as the AC is constantly under the mean stress, whereas dynamic load changes for different activities [1-3]. Upon analysis of published data and the models limitations, we may observe that purely elastic (Hookean) and viscous (Newtonian) models have to be properly combined to correspond to experimental data. Usually this is being done by application of several Kelvin and Maxwell spring-dashpot models, of which Zener (also known as standard linear solid) and Burgers models are the most comprehensive. Based on the experimental analysis with BEST method [6], we selected Burgers model as the best compromise,
which does not require assumption of relaxation times spectra and has a minimal set of fitting parameters. The Burger model consists of a linear spring and a linear dashpot in parallel (Kelvin element) and another linear spring and linear dashpot in series (Maxwell element, [7]). In this model response equation reading as

\[ \sigma + p_1 \dot{\sigma} + p_2 \ddot{\sigma} = q_1 \dot{\epsilon} + q_2 \ddot{\epsilon} \]  

(1.1)

where \( \sigma \) is stress, \( \epsilon \) is strain for one-dimensional loading. Using \( E \) for the moduli of elasticity (spring elements) and \( \eta \) for the viscosities (dashpot elements), we can write

\[ p_1 = \tau_1 \left[ 1 + \frac{E_1}{E_2} \right] + \tau_2, \quad p_2 = \tau_2, \quad q_1 = \tau_2 E_1, \quad q_2 = \tau_2 \eta_2, \quad \tau_1 = \frac{\eta_1}{E_1}, \quad \tau_2 = \frac{\eta_2}{E_2}, \]  

(1.2)

where \( \tau_i \) are the relaxation times. The creep function connects the strain and stress by the functional relation

\[ \epsilon = cr \cdot \sigma \]  

(1.3)

After solving the equations (1.1), (1.3) comes as

\[ cr = \frac{1}{E_1} \left( 1 + \frac{t}{\tau_1} \right) + \frac{1}{E_2} \left[ 1 - \exp \left( -\frac{t}{\tau_2} \right) \right]. \]  

(1.4)

This result is well-known in materials engineering especially for creep of solids with substantial viscosity component. Applying this equation to porous fibrous scaffold under creep conditions, relevant to the implant use [6], we found an excellent fit of the data in both wet and dry cases, Figure 2. Despite the parameters used in (1.2) are different for these two cases, the model predicts well behavior of the specimens, which is also reproducible in the experimental setup. It was observed that parameters with the model equations (1.2 and 1.4) are not exactly the materials constants, but they depend on the applied load (stress), and in this sense this Burgers model becomes non-linear.

![Figure 2](image)

Figure 2. Experimental data (creep function vs. time in seconds) for porous scaffolds under 0.8 N load and the Burgers model fit for dry (left) and wet (right) conditions.

### 3. Numerical simulation and the experimental validation

The evidence of reasonable Burgers model fit for creep response allows calculations of the dynamic response of the scaffold under prescribed loading, which might simulate realistic knee joint operations. Here COMSOL software was used for such analysis, although other FEA algorithms can be also applied. The scaffolds were subjected to dynamical mechanical analysis (DMA) under 1 Hz oscillating load with a contacts part which is responsible for creep behavior for about 5 h experiment. Obtained
axial strain values were compared with the FEA simulations along the axial symmetry axis for different models. Figure 3 show experiment data with linear (red) and non-linear Burgers model predictions, which clearly shows that non-linearity effects result in better prediction of materials behavior especially for long time scale.

![Figure 3. DMA of the scaffold disk specimen and modeling predictions for axial strain vs. time (s).](image)

4. Discussion

Characterization of the visco-elastic behavior of the biomaterials can be achieved with different models, which basic elements could be combined with high complexity. However, whereas large number of virtual springs and dashpots could be calculated as in Weichert model [8], this does not allow reverse design of the scaffold with minimal number of parameters, which could be determined in a simple creep experiment and later expand to dynamic loading conditions.

In this work we have demonstrated that adding a simple non-linearity into Burgers model allows a very good description of the material behavior. This results in two important practical outputs. First, biomechanical conditions of the patient allow formulation of scaffold properties in terms of parameters (1.2) as functions of expected loads. Second, biomaterial manufacturers could make a fast screening of potential candidates to determine these parameters and thus predict how well particular structure and properties of the material would fit clinical demands.

Acknowledgement. Financial support from the Finnish National Agency for Innovations (Tekes) under project No. 211493 is gratefully acknowledged.

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