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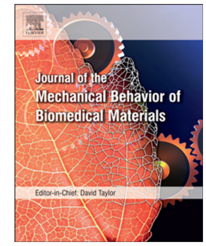

Research Paper

The anisotropic mechanical behaviour of electro-spun biodegradable polymer scaffolds: Experimental characterisation and constitutive formulation

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ABSTRACT

Electro-spun biodegradable polymer fibrous structures exhibit anisotropic mechanical properties dependent on the degree of fibre alignment. Degradation and mechanical anisotropy need to be captured in a constitutive formulation when computational modelling is used in the development and design optimisation of such scaffolds.

Biodegradable polyester-urethane scaffolds were electro-spun and underwent uniaxial tensile testing in and transverse to the direction of predominant fibre alignment before and after in vitro degradation of up to 28 days. A microstructurally-based transversely isotropic hyperelastic continuum constitutive formulation was developed and its parameters were identified from the experimental stress–strain data of the scaffolds at various stages of degradation.

During scaffold degradation, maximum stress and strain in circumferential direction decreased from 1.02 ± 0.23 MPa to 0.38 ± 0.004 MPa and from $46 \pm 11\%$ to $12 \pm 2\%$, respectively. In longitudinal direction, maximum stress and strain decreased from 0.071 ± 0.016 MPa to 0.010 ± 0.007 MPa and from $69 \pm 24\%$ to $8 \pm 2\%$, respectively. The constitutive parameters were identified for both directions of the non-degraded and degraded scaffold for strain range varying between 0% and 16% with coefficients of determination $r^2 > 0.871$. The six-parameter constitutive formulation proved versatile

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enough to capture the varying non-linear transversely isotropic behaviour of the fibrous scaffold throughout various stages of degradation.

1. Introduction

Regenerative medicine has emerged as one of the most dynamic drivers in the development of advanced engineered biomaterial solutions for tissue engineering applications (Furth et al., 2007; Williams, 2006). One crucial element in regenerative medicine is scaffolds that facilitate and guide the engineering and regeneration of biological tissues according to the application.

Scaffolds need to be designed so as to promote engineering and regenerating tissue such that the newly created tissue biologically and mechanically mimics the healthy host tissue (Furth et al., 2007). In the treatment of cardiovascular diseases, applications for regenerative medicine include tissue regenerative small-diameter vascular grafts which remain one of the major challenges to date (Zilla et al., 2007). In such grafts, porosity is a key factor for the long term success (Zilla et al., 2007). One method of introducing porosity in scaffolds for the engineering of soft biological tissues, such as vascular tissue, is electro-spinning of polymers (Braghirolli et al., 2014; Rocco et al., 2014). This technology results in fibrous polymeric networks. Process parameters allow controlling the degree of alignment of the fibres (Ayres et al., 2007; Wu et al., 2010) – a parameter that affects the mechanical properties of the scaffold. Scaffolds with fibres randomly distributed typically exhibit similar properties in different directions whereas the alignment of fibres predominantly in one direction introduces mechanical anisotropy (Ayres et al., 2007). Electro-spun scaffolds with a high degree of fibre alignment exhibit a higher elastic modulus, i.e. stiffness, in fibre direction and a lower elastic modulus perpendicular to the fibre direction. The directional mechanical properties of the scaffold can be utilised to tailor the structural properties of the engineered tissue. They add, however, complexity to the design process which needs to be adequately addressed.

Regeneration of biological tissues without any synthetic material remaining in the engineered construct can be facilitated with scaffolds materials that degrade in vivo. The degradation of the scaffold material introduces a transient process that affects the structural properties of the scaffold (Dargaville et al., 2013; Krynauw et al., 2011) and consequently engineering tissue (Roh et al., 2008). It is important to ensure that the degradation of the scaffold does not lead to premature failure of the tissue construct e.g. when the scaffold's disintegration rate is not adequately balanced with the rate of tissue ingrowth.

When computational modelling is utilised to assist in the development of tissue-regenerative scaffolds and tissue-engineered constructs, the numerical representation of the mechanical and structural properties of the scaffold, and the changes thereof described above, is imperative. It is therefore essential to have access to appropriate constitutive models (or constitutive laws) which, in a purely mechanical context, are sets of mathematical equations relating stress to strain. These mathematical relations can then be implemented in a computational environment, typically a finite element application, to subsequently carry out mechanical simulations on tissue engineering constructs for various loading scenarios and operating conditions.

To computationally model the mechanical response of a polymer-based fibrous scaffold one could take a *microstructural* or *phenomenological* approach. In the former approach, the geometry of the electro-spun fibres would be explicitly modelled and assigned isotropic properties of the bulk polymer material. In that case, mechanical anisotropy of the scaffold would arise as a consequence of its structural properties. The second modelling approach would consider the fibrous scaffold as a single bulk structure made of a homogeneous material, therefore disregarding the explicit geometry of polymer fibres. A constitutive model capturing the physical transversely isotropic behaviour of electro-spun fibre scaffold would then be assigned to the scaffold which would effectively be modelled as a macroscopic structure governed by a macroscopic phenomenological constitutive law. In this work, the latter approach is pursued and is described in Section 3.

Biodegradable polymers used for medical device, tissue engineering and regenerative medicine applications typically operate in complex conditions whether it is from the viewpoint of the biochemical or mechanical environment (Riboldi et al., 2005; Soares et al., 2010b). Structures made of biodegradable polymers generally are subjected to strain rate-sensitive cyclic loads sufficient to induce large elastic and/or inelastic strains operating in the non-linear regime (Grabow et al., 2013; Vieira et al., 2014, 2013). It is therefore important to consider constitutive models that, depending on particular applications, can capture specific features such as large deformations. For example, in that case, this consideration rules out Hooke's elasticity as a suitable constitutive model. Of course, a key feature of biodegradable polymers is their inherent propensity to have their mechanical strength reduced as a result of chemo-mechanical damage. Several constitutive models accounting for these phenomena have been proposed.

Notably, Soares et al. (2007, 2010c) and Soares and Zunino (2010b) developed 3D constitutive models based on hyperelastic potentials combined with damage laws to represent deformation-induced hydrolysis (Soares et al., 2010c). They also proposed a mathematical mixture model capturing water-dependent degradation and erosion as well as drug release (Soares and Zunino, 2010a).

In the study by Vieira et al. (2011), several hyperelastic strain energy functions were assessed to represent the purely mechanical behaviour of biodegradable aliphatic polyester