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Evolutional growth and remodeling in multiphase living tissue

T. Ricken [a,*], J. Bluhm [b]

[a] Computational Mechanics, University of Duisburg-Essen, Campus Essen, 45117 Essen, Universitätsstr. 15, Germany
[b] Institute of Mechanics, University of Duisburg-Essen, Campus Essen, 45117 Essen, Universitätsstr. 15, Germany

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ABSTRACT

It is well-known that biological systems have the capacity to change their inner structure and shape for an optimized load transfer. This paper deals with the development of a multiphase model to describe the growth and remodeling phenomenon in biological systems in order to learn more about the biological optimization mechanisms. A continuum triphasic model (i.e., a solid having interstitial space filled with water containing nutrients) based on the multiphase Theory of Porous Media (TPM) is proposed to provide a thermodynamically consistent description of the growth and remodeling phenomenon. The constitutive modeling of stress–strain- or nutrient-driven growth and remodeling phenomena is discussed. Finally, the influence of different driving mechanisms for growth is demonstrated by three illustrative exemplary problems.

1. Introduction

Living tissue consists of different phases and components in solutions. Even in the case that all interactions between these ingredients are known, and that is by far not the case, the solution of the coupled system of equation is not feasible. From this we divide the tissue into three different main groups; a solid phase, a fluid phase and a nutrient phase. All existing phases and components are subgroups of the defined main groups. Although the division is coarse, the model allows a deeper understanding in the functionality of the tissue, especially in contrast to a one-component approach. Fist of all, the apparent viscoelasticity of tissue is a combination of a fluid flow-dependent and a fluid flow-independent mechanism, see i.e., DiSilvestro and Suh [12], and that is obviously not describable using a one-component approach. Secondly, the remodeling and growth processes underly the restriction of mass transfer and phase transition. It is impossible to balance the mass exchange and control the phase transition by using an open system approach with a one-component material. Although the proposed three phase model is far from capturing all the mechanisms that occur during the phase transition, it provides a more detailed insight into the functionality of living tissue.

In general, growth and remodeling in living tissue are continuous processes and the results of a time dependent phase-conversion between tissue cells and nutrients, by which the nutrients themselves can be transported through the tissue. Overall, we consider that biological tissues consist mostly of multi-component materials, frequently exhibiting an anisotropic internal structure plus reaction to changing load cases with internal biological and/or chemical activities.

Growth processes in living tissues are driven by mechanical, chemical, genetic, metabolic, and hormonal influences. Due to the lack of detailed knowledge and specific parameters with which to quantify all these influences, a holistic numerical simulation cannot currently be provided. However, the capability of tissue to remodel its structure and density due to a changing stress state has been well-known for over a century. The precondition for tissue growth is the existence of growth material like nutrients. Therefore, a triphasic calculation concept for the description of stress and nutrient induced growth based on the well established Theory of Porous Media will be presented in this paper.

In terms of comprehensive overviews of the experimental findings of the growth phenomenon, the reader refers to, e.g., Fung

* Corresponding author. Tel.: +49 201 1832681; fax: +49 201 1832680.
E-mail address: tim.ricken@uni-due.de (T. Ricken).

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[16,17] and Taber [26]. An overview of different models for the description of growth phenomena can be found in Ricken et al. [23]. For one-component approaches, the latest findings on mechanical regulation of morphogenesis are presented in Taber [27]. Fundamentals on the Theory of Porous Media can be found in Biot [2–4], Bowen [10,9], Ehlers [13,14], de Boer [8] or Bluhm [6].

A question get to be answered is the determination of the right mechanical stimulus on the growth. Proper candidates are strain or strain state. The purpose of the present study is to explore how growth reacts on different stimuli. Therefore, we present three different numerical examples where we compare the influence of the mechanical stimuli on the growth mechanism.

2. Basic model and assumptions

In the developed model we apply the aforementioned Theory of Porous Media (TPM) which is composed of the classical Mixture Theory and the concept of volume fraction. In the following section, the basics of this theory will be sketched shortly and not completely. For a deeper introduction we refer to e.g., de Boer [8] or Ehlers [14].

The examined porous body $\varphi = \sum \varphi^\alpha$, $\alpha \in \{S = \text{Solid}, L = \text{Liquid}, N = \text{Nutrients}\}$, consists of a porous solid phase φ^S which is saturated by a fluid. The fluid itself is composed of φ^L (liquid) and φ^N (nutrients), see Fig. 1. The bulk material is made up of the three components, where the volume fractions n^α refer the volume elements dv^α of the individual constituents φ^α to the bulk volume element dv with

$$n^\alpha(\mathbf{x},t) = \frac{dv^\alpha}{dv}, \quad \sum_\alpha^{S,L,N} n^\alpha(\mathbf{x},t) = \sum_\alpha^{S,L,N} = \frac{\rho^\alpha}{\rho^{\alpha R}} = 1, \tag{1}$$

where $\mathbf{x}$ is the position vector of the spatial point x in the actual placement and t is the time. The volume fractions n^α in $(1)_1$ meet the volume fraction condition $(1)_2$ for κ constituents φ^α. Furthermore, the partial density $\rho^\alpha = n^\alpha \rho^{\alpha R}$ of the constituent φ^α is related to the real density of the materials $\rho^{\alpha R}$ involved via the volume fractions n^α, see $(1)_2$.

The saturated porous solid will be described as an immiscible mixture of all constituents φ^α with particles $\mathbf{X}_\alpha$. Consequently, we introduce independent Lagrangian motion functions $\mathbf{x} = \chi_\alpha(\mathbf{X}_\alpha, t)$ and $\mathbf{X}_\alpha = \chi_\alpha^{-1}(\mathbf{x}, t)$, deformation gradients $\mathbf{F}_\alpha = (\partial \mathbf{x})/(\partial \mathbf{X}_\alpha) = \text{Grad}_\alpha \chi_\alpha$ and Jacobian $J_\alpha = \det \mathbf{F}_\alpha$ for each constituent.

The local statements of the balance equations of mass are given for the constituents φ^α by

$$(\rho^\alpha)'_\alpha + \rho^\alpha \text{div} \mathbf{x}'_\alpha = \hat{\rho}^\alpha, \tag{2}$$

and the local statements of the balance equations of momentum read as follows

$$\text{div} \mathbf{T}^\alpha + \rho^\alpha(\mathbf{b} - \mathbf{x}''_\alpha) + \hat{\mathbf{p}}^\alpha - \hat{\rho}^\alpha \mathbf{x}'_\alpha = \mathbf{o}. \tag{3}$$

In (2) and (3), 'div' denotes the spatial divergence operator, $\hat{\rho}^\alpha$ represents the mass supply between the phases which must conform to

$$\hat{\rho}^S + \hat{\rho}^L + \hat{\rho}^N = 0, \tag{4}$$

$\mathbf{T}^\alpha$ is the partial Cauchy stress tensor, $\rho^\alpha \mathbf{b}$ specifies the volume force and $\hat{\rho}^\alpha$ describes the interaction forces of momentum of the constituents φ^α which are restricted to

$$\hat{\mathbf{p}}^S + \hat{\mathbf{p}}^L + \hat{\mathbf{p}}^N = \mathbf{o}. \tag{5}$$

In the further description, the system is investigated under the condition of a materially incompressible mixture-body

$$(\rho^{SR})'_S = 0, \quad (\rho^{LR})'_L = 0, \quad (\rho^{NR})'_N = 0, \tag{6}$$

which leads us to the conclusion that the volumetric deformations are only a result of the change in the porosity, i.e., from the volume fraction n^S. In this approach, energy transfer will be neglected between all phases as well as accelerations ($\mathbf{x}''_\alpha = \mathbf{o}$).

3. Constitutive modelling

For the proposed three phase model the overall entropy inequality, enlarged by the material time derivative of the saturation condition and the balance equations of mass, both multiplied with the corresponding Lagrange multiplier, has been elaborated on in Ricken and Bluhm [20,21]. From that, we obtain necessary and sufficient conditions for the unrestricted validity of the second law of thermodynamics. The following set of constitutive relation is suggested based on this thermodynamic consistent framework.

3.1. Stress

The constitutive relations for the partial Cauchy stress tensors are proposed with

$$\begin{aligned} \mathbf{T}^S &= -n^S \lambda \mathbf{I} - (n^S)^2 \rho^{SR} \frac{\partial \psi^S}{\partial n^S} \mathbf{I} + 2\rho^S \mathbf{F}_S \frac{\partial \psi^S}{\partial \mathbf{C}_S} \mathbf{F}_S^T \\ &= -n^S \lambda \mathbf{I} - (n^S)^2 \rho^{SR} \frac{\partial \psi^S}{\partial n^S} \mathbf{I} + \mathbf{T}_E^S, \end{aligned} \tag{7}$$

$$\mathbf{T}^F = -(n^L + n^N)\lambda \mathbf{I} = -n^F \lambda \mathbf{I}, \quad n^F = n^L + n^N, \tag{8}$$

where $\mathbf{T}_E^S$ is the effective stress, see e.g., Bishop [5] or Skempton [24], $\mathbf{T}^F$ is the fluid stress tensor and λ denotes the fluid pressure. For the formulation of the anisotropic constitutive relations we use the concept of integrity-bases which allows a coordinate-invariant formulation, see, e.g., Spencer [25], Boehler [7], Betten [1] or Zheng and Spencer [28,29]. In this model we restrict ourselves to a transversely isotropic material response and use the stored energy function presented in Ricken et al. [23]. In the end, this leads to an additive decomposition of the solid Helmholtz free energy function into an isotropic part, ψ_{iso}^S, and a transversely isotropic part, ψ_{ti}^S, i.e.,

$$\psi^S = \left(\frac{n^S}{n_{0S}^S}\right)^n \psi_{iso,neo}^S(I_1, I_2, I_3) + \psi_{ti}^S(J_4, J_5). \tag{9}$$

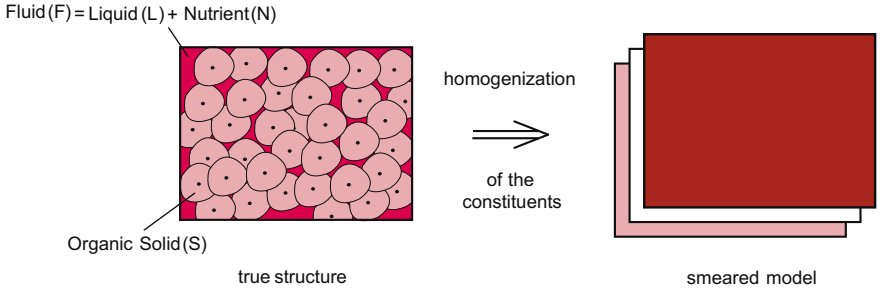

Fig. 1. Homogenization.