Modelling mass transport in morphogenetic processes: a second gradient theory for growth and material remodelling

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Abstract

Growth and remodelling are strictly interlaced in the biological tissues and their unified treatment is a challenge in continuum mechanics, where the evolution of macroscopic quantities, like shape and stresses, are dictated by the non-equilibrium transport and reaction equations of biochemicals at the microscale. Here we derive the kinematic description and the main balance equations of a second gradient theory aimed at modelling both volumetric growth and mass transport inside the living matter. Thermodynamical arguments suggest defining few admissible classes of constitutive theories, which model the diffusive growth processes inside a continuum body. In addition, we propose evolution equations for first and second gradient inhomogeneities, considering different symmetry groups and initial second-order symmetries. Few examples of morphogenetic models will be presented, in order to show the biomechanical importance of coupling volumetric growth, mass transport and internal stress state in physiological and pathological conditions for biological matter.

Keywords: morphogenesis, mass transport, second gradient theory, configurational forces, growth, remodelling

1. Introduction

Morphoelastic theories aim at modelling the emergence of shapes in biological matter, a process that occurs at different spatial scales, starting from the molecular level. According to the definition of Taber [1], morphogenesis can be defined as the final result of all those processes involving an interaction between growth (i.e. a change in mass) and remodelling (i.e. a change in material properties). Typical examples of morphogenetic processes happen at the embryonic stage, when growth patterns start the differentiation of organs, in wound healing and in tissue regeneration. The simultaneous treatment of growth and remodelling is a challenge in continuum mechanics, where a multiscale approach is needed for coupling macroscopic growth rate and stress with the local biochemical processes, in view of producing the macroscopic shape. If continuum theories can successfully describe the mechanics of volumetric growth in uniform bodies, a satisfactory constitutive description of mass transport phenomena in biological matters is still lacking. Transport of nutrients and morphogens are usually modelled by means of systems of reaction-diffusion equations, without the due coupling with the stress field and with poor thermomechanical consistency. On the other hand, transport phenomena are paramount in developmental biology, where gradients of morphogens dictate the generation of complex patterns [2]. Here we propose a unifying constitutive theory, involving the second gradient of deformation, in order to couple mass transport and volumetric growth.

2. Second gradient theory of growth and mass transport

The aim of this section is to introduce the proper kinematical description and the basic balance principles necessary to define a second gradient theory for volumetric growth and mass transport, inside a continuum body.

2.1. Direct and inverse kinematic descriptions

Let us consider a mapping $\mathbf{x}=f(\mathbf{X},t)$ that provides the actual position $\mathbf{x}$ of a material point of a continuum body at time t, with position $\mathbf{X}$ in the reference configuration. The deformation field is described through the tensor gradient of deformation $\mathbf{F}=\text{Grad}\ \mathbf{x}=\nabla_X \mathbf{x}$, and the second gradient of the deformation $\nabla_X\mathbf{F}=\nabla_X\nabla_X\ \mathbf{x}$. The mechanical problem for volumetric growth and mass transport can be formulated in material and spatial references, using two different space-time parametrizations: the so-called direct and inverse kinematics, respectively. The direct kinematics is based on the set of variables $(\mathbf{X},t)$ belonging to the physical space, and the equations involves the spatial velocity $\mathbf{v}=\partial\mathbf{x}/\partial t|_X$, and the material (spatial) velocity gradient $\mathbf{l}=\partial\mathbf{F}/\partial t|_X$ $(L=\partial\mathbf{F}/\partial t|_X\ \mathbf{F}^{-1})$. On the other hand, the inverse kinematics is based on the inverse motion $\mathbf{X}=f^{-1}(\mathbf{x},t)$, where the material domain changes over time keeping its range fixed. When dealing with inhomogeneities (or pseudo-inhomogeneities, in a more general framework) in the material setting, the theory of configurational forces demonstrates that the spatial parameterization is unable to account for all the degrees of freedom associated to the deformation fields [3]. In particular, the physical linear momentum density $\mathbf{p}$, conjugated to the spatial velocity $\mathbf{v}$, is uniquely associated to the translational momentum. In the material manifold, the inverse motion velocity $\mathbf{V}$ can be defined through the identity:

$$d\mathbf{X}/dt=\partial f^{-1}(\mathbf{x},t)/\partial t+\partial f^{-1}(\mathbf{x},t)/\partial\mathbf{x}\cdot\partial\mathbf{x}/\partial t|_X=\mathbf{V}+\mathbf{F}^{-1}\mathbf{v}=0. \quad (1)$$

The balance of conjugated momentum $\mathbf{P_m}$, also referred as pseudo-momentum density or canonical energy-momentum density, must be considered in problems involving local rearrangements of the material manifold. If we want to model the presence of a mass transport (e.g. due to diffusive growth processes), such a mass flow in the material configuration is coupled to the referential inverse-velocity gradient:

$$\nabla_X\ \mathbf{V}=-\nabla_X\ (\mathbf{F}^{-1}\mathbf{v})=-\mathbf{F}^{-1}\mathbf{L}\mathbf{F}+\nabla_X\ \mathbf{F}^{-1}\cdot\mathbf{F}\mathbf{V}. \quad (2)$$

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Equation (2) relates the direct and the inverse velocity gradients in terms of the second gradient of the deformation field. As previously discussed in [4], a second gradient morphoelastic theory is therefore necessary to provide a constitutive equation for the mass transport, as well as to define thermodynamically compatible evolution equations for mass remodeling during the morphogenetic processes.

2.2. Balance principles

A continuum treatment of growth must account for volumetric formation and/or absorption of mass (through a source/sink term Γ in the balance equation in the reference configuration) as well as for the surface flow, defined by a flux **M**. The balance of mass in the material manifold is expressed in function of the time derivative of the reference density ρ_o at the material point in **X**:

$$\partial\rho_o /\partial t\,|_X = \Gamma(c_i)\,\rho_o + \nabla_X \cdot \mathbf{M}(\mathbf{F}, \nabla_X \mathbf{F}, c_i). \tag{3}$$

The time and space characteristics of growth in living materials are typically driven by the evolution of the concentration of the passive scalars fields c_i, $i=1,....n$. In terms of configurational forces, such scalar fields can be treated as internal variables in the expression of the free energy W of the system:

$$W = \Psi(\mathbf{F}, \nabla_X \mathbf{F}, c_i; X). \tag{4}$$

Here an explicit dependence on **X** is considered (so that the material can be *smoothly* material inhomogeneous), while we drop an explicit dependence on time, and phenomena like ageing are discarded. The scalars $c_i(\mathbf{X},t)$ can be seen as the concentration per unit of volume of chemical substances and/or signals (e.g. nutrients, growth factors, morphogens) which are dispersed in the interstitial liquid during the morphogenetic processes [5]. We therefore include a balance equation, for each *i-th* species, having the following material form:

$$\partial c_i /\partial t\,|_X = \boldsymbol{\zeta}_\iota(\mathbf{F}, \nabla_X \mathbf{F}, \rho_o, c_i) + \nabla_X \cdot \mathbf{j_i}(\mathbf{F}, \nabla_X \mathbf{F}, c_i). \tag{5}$$

The fluxes $\mathbf{j}_i$ depend on the free energy, in a way to be determined on the basis of thermodynamical arguments; the source terms $\boldsymbol{\zeta}_\iota$ represent the local absorption rates inside the continuum body, which accounts for second gradient effects (e.g. curvature-dependent effects in the absorption of angiogenetic factors [6]). The Lagrangian form for the balance of linear momentum in direct kinematics can be expressed as follows:

$$\partial(\rho_o\,\mathbf{v})/\partial t\,|_X = \partial\,\mathbf{p}/\partial t\,|_X = \mathbf{b}_0 + \Gamma(c_i)\,\rho_o\,\mathbf{v} + \nabla_X \cdot (\mathbf{P} + \mathbf{v}\otimes\mathbf{M}) \tag{6}$$

where $\mathbf{b}_0$ represents the body forces, **P** is the first Piola-Kirchhoff stress tensor and $\otimes$ is the dyadic product. As discussed in the previous section, a more suitable formulation to describe the evolution of material inhomogeneities, as the ones due to volumetric growth and mass transport, requires to introduce the pseudo-momentum vector $\mathbf{P_m} = \rho_o\,\mathbf{F^T F V}$. The balance equation for $\mathbf{P_m}$ can be obtained by a canonical projection of eq.(6) in the material setting. Using the mass balance equation (4), such a projection can be written as:

$$\partial\,\mathbf{P_m} /\partial t\,|_X = \mathbf{f}_0 + \mathbf{f}_g + \mathbf{f}_{mt} + \mathbf{f}_{inh} + \mathbf{f}_c + \nabla_X \cdot \boldsymbol{\Sigma} \tag{7}$$

where:

$$\mathbf{f}_0 = -\mathbf{F^T b_0} \tag{8}$$

$$\mathbf{f}_g = \Gamma(c_i)\,\mathbf{P_m} \tag{9}$$

$$\mathbf{f}_{mt} = (\mathbf{P_m}/\rho_o)\nabla_X \cdot \mathbf{M} - \mathbf{F^T F}\,(-\nabla_X \mathbf{V} + \nabla_X \mathbf{F^{-1}} \cdot \mathbf{F}^{-T}\,\mathbf{P_m}/\rho_o)\mathbf{M} \tag{10}$$

$$\mathbf{f}_{inh} = \partial\,(1/2\rho_o\mathbf{v}^2 - \Psi)\,/\partial\mathbf{X}\,|_{\text{expl (fixed } \mathbf{F}, \nabla X\,\mathbf{F}, c_i)} \tag{11}$$

$$\mathbf{f}_c = -\,\Sigma_{j=1,...,i}\,(\,\partial\Psi/\partial c_j \cdot\nabla_X c_j) \tag{12}$$

The conservation of the pseudo-momentum in eq.(7) states that there are five sources of material inhomogeneities: the convection of the body forces ($\mathbf{f}_0$), the volumetric growth ($\mathbf{f}_g$), the mass transport ($\mathbf{f}_{mt}$), the true material inhomogeneties ($\mathbf{f}_{inh}$), and the internal variables ($\mathbf{f}_c$).

The material Eshelby tensor $\boldsymbol{\Sigma}$ is defined as follows:

$$\boldsymbol{\Sigma} = \boldsymbol{\Sigma}_\mathbf{f} - \nabla_X \cdot \boldsymbol{\Sigma}_\mathbf{s}\,, \tag{13}$$

where

$$\boldsymbol{\Sigma}_\mathbf{f} = -(1/2\rho_o\mathbf{v}^2 - \Psi) - \mathbf{F^T}\partial\Psi/\partial\mathbf{F} - \mathbf{2}(\nabla_X \mathbf{F})^\mathbf{T} : \partial\Psi/\partial(\nabla_X\mathbf{F}), \tag{14}$$

$$\boldsymbol{\Sigma}_\mathbf{s} = \mathbf{F^T}\,\partial\Psi/\partial(\nabla_X\mathbf{F}), \tag{15}$$

are the stress measures which drives the evolution of the first gradient and the second gradient material inhomogeneities, respectively.

3. Discussion and conclusion

In this communication we have sketched the derivation of the kinematic description and of the main balance equations for a second gradient theory of volumetric growth and mass transport in living matter. Thermodynamical considerations yield to define few classes of constitutive theories which couple stress and diffusive growth inside a continuum body. In addition, evolution equations for first and second gradient inhomogeneities can be proposed on the basis of different symmetry groups and initial second-order symmetries. Few examples of morphogenetic models will be presented in order to show the biomechanical importance of coupling volumetric growth, mass transport and internal stress state in physiological and pathological conditions for biological matter.

The same issue discussed herein has been addressed in the past within the multiphase framework. In contrast, this is the first constitutive model of mass transport within a growing one-phase continuum body. The continuum formulation in the material setting does not have the drawbacks of mixture theories, namely the ones related to the split of the partial stresses between the phases and to physically meaningful boundary conditions. Finally, such characteristics make the proposed modelling approach more suitable for computational applications in biomechanics.

References

[1] Taber, L.A. Biomechanics of growth, remodelling and morphogenesis. *Appl Mech Rev*. 48, pp. 487-545, 1995.

[2] Wolpert, L. Positional information and the spatial pattern of cellular differentiation. *J Theor Biol*. 25, pp. 1-47, 1969.

[3] Maugin, G.A., *Configurational forces: thermomechanics, physics, mathemathics and numerics*. first ed., CRC Press Taylor and Francis, 2010.

[4] Epstein, M. and Maugin, G.A. Thermomechanics of volumetric growth in uniform bodies, *Int. J. Plasticity,* 16, pp. 951-978, 2000.

[5] Ambrosi, D. and Guillou, A. Growth and dissipation in biological tissues. *Continuum Mech Therm* 19(5), pp.245-251, 2007

[6] Levine, H.A., Pamuk, S., Sleeman, B.D. and Nilsen-Hamilton, N. Mathematical modelling of capillary formation and development in tumour angiogenesis: penetration into the stroma, *Bull Math Biol,* 63, pp. 801-863, 2001.