"THERMOELASTIC" MODEL OF TISSUE GROWTH

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INTRODUCTION

Though the early works on growth were kinematical (Thompson [1]), using continuum mechanics is now widely accepted for describing growth, remodeling, and morphogenesis (Taber [2]). Since the work of Hsu [3], there appeared various models of growth: Cowin and Hegedus [4]; Klisch et al. [5]; Kuhn and Hauger [6]; Rodrigues et al. [7]; Skalak [8]. Multiplicative decompositions of the displacement gradient underlie many publications on analytical modeling of growth. In this case an intermediate configuration is introduced where the free deformation-growth is considered in the vicinity of every material point. Geometrical compatibility of the grown material particles is ensured by additional deformation and stress. Another line of the growth modeling is presented by Kuhn and Hauger [6], in which tissue is considered as a classical mixture of solid and fluid. These authors show that several well-known models of the adaptive growth can be embedded in their general theory.

Mathematical description of existing approaches is rather sophisticated and it includes variables that may be difficult to interpret in simple terms and to assess in measurements. In the present work a simple phenomenological theory of growth is formulated based on two measurable variables- displacements and mass densities. It is assumed that deformation and mass flow can describe growth of living tissues. The complete law of mass balance is coupled with the law of momentum balance. A constitutive model reflecting the physical similarity between thermal expansion and growth supplements these field equations. As in the case of the classical thermoelasticity the growth process is assumed to be quasi-static and small deformations are considered only. As a consequence of the imposed restrictions we obtain the uncoupled mass flow – deformation problem, which is almost entirely analogous to thermoelasticity. The proposed theory is examined by modeling growth of living cylindrical and spherical bodies. It is shown that the theory accommodates materials that can freely and homogeneously grow without generating stresses.

ANALYTICAL MODEL OF GROWTH

In spatial description the governing field and constitutive equations can be written as follows:

$$\frac{\partial \rho}{\partial t} = \mathrm{div}(\boldsymbol{\psi} - \rho \boldsymbol{v}) + \xi \,, \quad \frac{\partial (\rho \boldsymbol{v})}{\partial t} = \mathrm{div}(\boldsymbol{\sigma} - \rho \boldsymbol{v} \otimes \boldsymbol{v}) + \rho \boldsymbol{b} \,, \quad \boldsymbol{\sigma} = \boldsymbol{\sigma}^T \qquad (1,2,3)$$

$$\boldsymbol{\psi} = \hat{\boldsymbol{\psi}}(\rho, \nabla \rho, \boldsymbol{F}) \,, \quad \boldsymbol{\sigma} = \hat{\boldsymbol{\sigma}}(\rho, \nabla \rho, \boldsymbol{F}) \,, \quad \xi = \hat{\xi}(\rho, \nabla \rho, \boldsymbol{F}) \qquad (4,5,6)$$

where ρ is mass density; $\boldsymbol{\psi}$ is a vector of *mass flow*; ξ is mass supply per unit volume; $\boldsymbol{v}$ is velocity; $\boldsymbol{\sigma}$ is the Cauchy stress tensor; $\boldsymbol{b}$ is a vector of body forces per unit mass; $\boldsymbol{F}$ is the deformation gradient. Equations (1), (2), (3) represent balance of mass, linear and angular momentum accordingly, while equations (4), (5), (6) are constitutive relations of *simple growing materials*.

It should be emphasized that the full-scale local mass balance is considered in Eq. (1). The first term on the right hand side of this equation represents mass diffusion. This term manifests continuum. Dropping this term from Eq. (1) is analogous to dropping the divergence of the stress tensor from Eq. (2): in both cases we would get a collection of material points instead of a continuous medium. The vector of mass flow $\boldsymbol{\psi}$ appears after applying Cauchy tetrahedron argument to the mass supply per unit surface $\phi = \boldsymbol{\psi} \cdot \boldsymbol{n}$, where $\boldsymbol{n}$ is a unit normal to the surface.

In order to specify the described general framework analogously to the classical thermoelasticity the following restrictions are imposed: (a) the process is quasi-static, i.e. time-dependence is ignored; (b) deformations are small and body forces are ignored. The first restriction leads to the following mass and momentum balance laws:

$$\mathrm{div}\boldsymbol{\psi} + \xi = 0 \,, \quad \mathrm{div}\boldsymbol{\sigma} = \boldsymbol{0} \qquad (7,8)$$

There is no difference between the spatial and material description because of the second restriction.

Introducing the infinitesimal strain measure as a symmetric part of the displacement gradient $\boldsymbol{\varepsilon} = (\nabla \boldsymbol{u} + \nabla \boldsymbol{u}^T)/2$, we define the following constitutive equations:

$$\boldsymbol{\sigma} = \lambda \boldsymbol{\delta} \mathrm{tr}\varepsilon + 2\mu\boldsymbol{\varepsilon} - (3\lambda + 2\mu)\alpha\rho\boldsymbol{\delta}\ ,\ \boldsymbol{\psi} = \beta\nabla\rho\ ,\ \xi = \omega - \gamma\rho \qquad (9,10,11)$$

$$\rho := \rho(\omega, \boldsymbol{x}) - \rho(0, \boldsymbol{x}) \qquad (12)$$

where λ and μ are the Lame coefficients; $\boldsymbol{\delta}$ is the second-order identity tensor.

Increasing *parameter of mass supply* $\omega > 0$ is analogous to a quasi-static mechanical load. In contrast to the latter, however, ω is controlled by the tissue itself and its proper determination requires experiments. The dimension of ω is a unit of mass per volume and time. Time is not involved directly in quasi-static problems and can be replaced by some conditional units as it was done with Newtons per volume for the body forces.

The *coefficient of growth expansion* $\alpha > 0$ determines how much the relative volume changes for a given increment in mass density. Its dimension is an inverse of a unit of mass.

The *mass conductivity of solid* $\beta > 0$ determines how much the mass supply changes for a given increment of the gradient of mass density. Its dimension is a unit of mass supply time length per mass density.

The *coefficient of mass supply* $\gamma > 0$ reflects the resistance of the tissue to accommodate new mass for growing mass density. The second term on the right-hand side of Eq. (11) 'brakes' mass supply when the density grows. The dimension of γ is the dimension of ω per a unit of mass density.

It is worth noting that all these coefficients are generally inhomogeneous and depend on $\boldsymbol{x}$.

The similarity between the two first constitutive laws of growth and thermoelasticity is obvious after replacing the mass density increment by the temperature increment; the mass flow vector by the vector of heat flux; the coefficient of growth expansion by the coefficient of thermal expansion; and the mass conductivity of solid by the thermal conductivity of solid. In this case Eq. (9) is nothing but the thermoelastic generalization of the Hooke's law, and Eq. (10) is just the Fourier law of heat conduction (see Boley and Weiner [9]). The constitutive law analogous to Eq. (11), however, is usually absent in thermoelasticity because of the lack of volumetric heat sources. The thermoelastic analogy allows better understanding parameters of the growth model. The vector of mass flow is analogous to the vector of heat flux. We feel the heat flow by changing temperature without directly defining what the heat is. The same is true for the mass flow. We 'feel' it by changing mass density without directly defining what it is.

Substituting Eqs. (10) and (11) in (7) and assuming $\beta = const$ we obtain:

$$\beta\nabla^2\rho - \gamma\rho + \omega = 0 \qquad (13)$$

Boundary conditions on the body surface take form $\rho = \overline{\rho}$ or $\boldsymbol{\psi} = \beta\nabla\rho = \overline{\boldsymbol{\psi}}$ where the over barred quantities are given. These quantities should be fitted from experiments.

Substituting solution of Eq. (13) in Eqs. (9) and (8) it is possible to find the volumetric change and the corresponding stress field. Though generally stresses or strains influence growth, it seems that the uncoupling is reasonable for small deformations. If one sets $\overline{\rho} = \omega/\gamma$ on the boundary, then the homogeneous increment of mass density is obtained ($\rho = \omega/\gamma$) and no stresses are expected for bodies without geometrical constraints and surface tractions. To illustrate this point we considered radial growth of a cylinder and a sphere within the developed theory. In the case of free homogeneous growth with $\rho = \omega/\gamma = \mathrm{const}$, which fits Eq. (13), we obtain $u = \alpha(1+\nu)r\omega/\gamma$, $\sigma_{rr} = \sigma_{\theta\theta} = 0$ for radial growth of a cylindrical living body and $u = \alpha r\omega/\gamma$, $\sigma_{rr} = \sigma_{\theta\theta} = \sigma_{\varphi\varphi} = 0$ for radial growth of a spherical living body. Here Lame coefficients are replaced by Young modulus E and Poisson ratio ν. Neither in the case of the free homogeneously growing cylinder nor in the case of the free homogeneously growing sphere the internal stresses appear.

CONCLUSIONS

The problem of establishing a simple analytical model of growth based on observable and experimentally measurable variables was addressed. For this purpose a novel theory of tissue growth was proposed. This theory is analogous to thermoelasticity where temperature is replaced by mass density. In order to solve the growth problem for the given living body, it is necessary first to find the distribution of mass density from the mass balance equation. The thermoelastic counterpart of this equation is equation of heat conduction. When the mass density distribution is known, it is possible to find deformation from the momentum balance accounting for the generalized Hooke's law. The latter manifests close resemblance between growth and thermal expansion. The examples of radial free growth of a living cylinder and a living sphere reveal the capacity of the theory to accommodate materials that can grow freely and homogeneously without generating stresses. It is important to emphasize that only displacements and mass densities should be measured in order to calibrate the proposed theory. Recent developments of computer vision techniques combined with the noninvasive densitometry (based, for example, on X-ray techniques) will allow for the calibration of the proposed analytical model and its further use in the analysis of tissue growth.

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