A unified mixture formulation for density and volumetric growth of multi-constituent solids in tissue engineering

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Highlights

\begin{itemize}
\item Unified mixture formulation for both growth at constant density and growth at constant volume.
\item Lagrange multiplier treatment of traction boundary conditions for mixture theory.
\item Constitutive model and numerical method for inter-constituent interactive force field.
\end{itemize}

Abstract

A unified computational method is developed for the modeling of growth in hard and soft biological tissues using a mixture theory approach. The model problem of tissue engineering is considered, whereby a polymeric scaffold is infused by cells and cross-linking proteins. In particular, the underlying scaffold or fibrous network is treated as an inert anisotropic material, and the cross-linking cells or proteins are treated as isotropic materials capable of growth. Both the cases of (i) growth at constant density and (ii) growth at constant volume are considered in order to encompass a broader range of biological response. The relative motions and interactions of the constituents are treated in a generalized sense through the incorporation of mass transfer and drag force terms, in contrast to constrained mixture theory wherein all constituents are constrained to move and deform in unison. Therefore, nodal interpolations are required for both the scaffold and cross-linking solid constituents, thereby modeling concurrent and coexisting constituents. Emphasis herein is placed on the consistent numerical solution procedure for the coupled system of momentum balance equations. Numerical simulations involving growth and relaxation are performed on representative volumes to highlight the features of the method.

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Keywords: Mixture theory; Growth; Lagrange multiplier; Thermodynamic framework; Interactive force
## Nomenclature

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
<th>Unit</th>
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<tr>
<td>(e^{(\alpha)})</td>
<td>Internal energy density</td>
<td>(m^2/s^2)</td>
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<tr>
<td>(e_s^{(\alpha)})</td>
<td>Energy supply</td>
<td>(N/(m^2\ s))</td>
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<tr>
<td>(J^{(\alpha)})</td>
<td>Jacobian, determinant of deformation gradient</td>
<td></td>
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<tr>
<td>(J_g^{(\alpha)})</td>
<td>Growth Jacobian determinant</td>
<td></td>
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<tr>
<td>(J_e^{(\alpha)})</td>
<td>Elastic Jacobian determinant</td>
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<tr>
<td>(K^{(\alpha)})</td>
<td>Kinetic energy</td>
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<td>(m_\phi^{(\alpha)})</td>
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<td>(t)</td>
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<td>(s)</td>
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<tr>
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<td>(\partial V)</td>
<td>Mixture domain boundary, spatial configuration</td>
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<td>(\gamma)</td>
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<td>(b)</td>
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<td>Spatial velocity gradient</td>
<td>(1/s)</td>
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<td>Elastic velocity gradient</td>
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<td>(l_g^{(\alpha)})</td>
<td>Growth velocity gradient</td>
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<td>First Piola–Kirchhoff stress, intermediate configuration</td>
<td>(N/m^2)</td>
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<tr>
<td>(q_e^{(\alpha)})</td>
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<td>(T)</td>
<td>Prescribed surface traction</td>
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<td>(t^{(\alpha)})</td>
<td>Surface traction, spatial configuration</td>
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Nomenclature

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<th>Variable</th>
<th>Description</th>
<th>Unit</th>
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<tr>
<td>$u^{(α)}$</td>
<td>Constituent relative velocity</td>
<td>m/s</td>
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<tr>
<td>$v^{(α)}$</td>
<td>Spatial velocity</td>
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<td>Material coordinate</td>
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<tr>
<td>$x$</td>
<td>Spatial coordinate</td>
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<td>$φ^{(α)}$</td>
<td>Deformation mapping function</td>
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<td>$ϕ$</td>
<td>Mixture deformation trace field</td>
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<tr>
<td>$λ^{(α)}$</td>
<td>Traction Lagrange multiplier</td>
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<td>$μ^{(α)}$</td>
<td>Lagrange multiplier weighting function</td>
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<td>$σ^{(α)}$</td>
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<td>$ψ$</td>
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1. Introduction

Biological tissues are complex, hierarchical structures composed of several materials that often possess anisotropic stiffness properties. Examples include skeletal, muscular, and intestinal tissues. Interest in quantitative modeling of these systems continues to increase, with end goals such as tissue and implant engineering. While these systems may be effectively modeled as continua, their distinguishing feature is that they grow and remodel under mechanical and chemical stimuli by exchanging mass with their environment. Proliferation and atrophy of cells and their associated extracellular matrices in response to persistent mechanical stimuli have been documented for hard tissues [1], soft tissues [2,3], and tumors [4]. For example, bone density increases with exercise, and blood vessel wall thickness and morphology may be affected by blood pressure and cardiac cycles. By constructing mechanical models of biological systems, the combined effects of internal stress as well as nutrients and other stimuli may be elucidated. Such knowledge can be applied to improve the design of scaffolds for tissue engineering to increase cell mobility and proliferation in targeted locations.

In order to practically model biological processes at the tissue scale, some degree of homogenization is typically employed to avoid the expense of resolving the microstructure but nonetheless preserving the distinct evolutionary character of each constituent. A suitable framework for homogenization is the so-called mixture theory, starting with the pioneering work of Truesdell and Noll [5] and subsequent refinement by other researchers [6,7]. Within mixture theory, each constituent is assumed to co-exist in a neighborhood of each material point of the deformable domain. The mixture is a closed thermodynamical system within which the constituents can grow and remodel. Applications of mixture theory for modeling biological processes involving solid and fluid constituents include tumor growth [8,9], turnover of collagen in tendons [10], triphasic cartilage mechanics [11], tissue engineering with polymeric scaffolds [12], interstitial tissue growth [13], and growth in the cardiovascular system [14,15]. Recent developments by Rajagopal and coworkers have focused on the concept of evolving natural configurations [16,17], such as the treatment of interstitial growth including matrix transport [18] and the development of homogenized constrained mixture theory [19] to reduce the extent of the natural configuration history to be retained during computational modeling.

A crucial aspect of each mixture model is the constitutive treatment of mass exchange (associated with growth) and momentum exchange (associated with interactive forces) as well as any constraints on the constituent kinematics [17]. Growth is most often treated as an evolution of constituent partial density rather than a local change in volume [6]. Developing appropriate constitutive models to account for motion of cells within the mixture and their response to environmental stimuli remains a significant challenge [12,20]. Also, the time scales of growth processes are often much longer than physiological load cycles, so that multiple time scales may need to be treated [15]. To simplify the framework, most mixture models for solid constituents employ the constrained mixture assumption, meaning that all constituents deform identically and have equal strain [15,17]. This assumption may be too restrictive if relative deformation and morphing is expected between the constituents in the microstructure. Presently, the development of numerical formulations for multi-constituent solid mixtures undergoing relative deformations and remodeling remains an open problem.
A simplified continuum approach compared to mixture theory has also emerged under the title of open system mechanics. The fundamental idea is that the body is treated as a single constituent that exchanges mass with its environment (through e.g. nutrient uptake) in addition to classical momentum and entropy exchange. In the open system context, the kinematics of growth is almost exclusively considered within one of two classes: density growth and volume growth [21]. The hypothesis of density growth, beginning with [1], is that new material is deposited in the existing constituent microstructure by filling in pores without disturbing the size of the infinitesimal material neighborhood. The governing thermodynamics [22] is then enhanced to track the evolution of density through the balance of mass equation, analogous to the evolution of partial density of constituents in mixture theory [6]. The density field may be treated as an internal degree of freedom if mass fluxes are considered or simply as an internal variable if growth occurs through mass sources alone [23]. Constitutive models for density evolution are typically stress-driven [24], although models based on strain energy density and homeostatic equilibrium have also been proposed [25]. Also, while most density growth formulations account for only isotropic functional adaptation, more recent approaches [26] have accommodated anisotropic functional adaptation through a formulation based on the micro-sphere concept.

In contrast, volume growth in open system mechanics, beginning with [27], hypothesizes that new material of constant density is deposited by an expansion of the infinitesimal material neighborhood. Herein, the growth kinematics is realized via a multiplicative split of the deformation gradient into elastic and growth phases, similar to finite strain elastoplasticity [28]. Based on the assumed form of the spatial velocity gradient of the growth deformation, various models for isotropic growth [29] and anisotropic growth [30,31] have been proposed to account for bulk change or preferential fiber orientation. Computational mechanics realizations of these models using the finite element method have been developed [32] and have been extended to model patient-specific geometries for arteries and cardiac muscle [33–35]. While most constitutive models are expressed through various large-deformation measures of stress, the Eshelby stress (expressed in the intermediate configuration) offers a particularly elegant way to relate growth to a mechanical stimulus [36]. These volumetric growth models have been elevated by [14,37–39] to accommodate both bounded and unbounded growth through the concept of a non-zero homeostatic internal stress.

Thus, several constitutive models have emerged for modeling growth in hard and soft tissues using open system mechanics [21,40]. However, few attempts have been made to unify the formulations for density growth and volume growth within a common thermodynamical framework. One noteworthy method has been proposed in [41] to accommodate simultaneous change in density and infinitesimal material neighborhood. Additionally, the single growing constituent framework of open system mechanics may not be well suited to modeling tissues composed of multiple dominant constituents. Particularly, for engineered tissues, the polymeric scaffold is an inert material while the surrounding cells and matrix exhibit growth and remodeling. If each constituent has unique mechanical properties, then the mechanical response at the tissue scale may exhibit an evolving degree of anisotropy as the relative mass progressively evolves. Such problems are amenable to treatment of multiple constituents within mixture theory.

In the present work, we develop a mixture theory for multiple deformable solids and a computational formulation based on finite elements for modeling growth in biological systems at the tissue scale. The mixture framework is built upon the developments for constrained mixture theory by Humphrey and Rajagopal [17], but crucially we relax the assumption of constrained deformation of the solid constituents as in Hall and Rajagopal [42] and Hall [43]. Additionally, the kinematics of growth is expressed in the intermediate configuration arising from a multiplicative split of the constituent deformation gradient. In this manner, the growth of the solid constituents is treated in a unified fashion enabling either density growth or volume growth to be modeled within the same framework. The general theory is applied to model a system consisting of a (inert) scaffold, (growing) matrix, and nutrients as a prototypical example of tissue engineering. Specific constitutive models are presented for anisotropic growth in a unidirectional fiber network reflecting either density growth or volume growth. The deformation field of each constituent is interpolated separately using finite elements in order to represent the homogenized effect of incompatibilities generated in the microstructure. The relative deformation of the constituents is controlled by the interactive force [42], expressed in terms of drag forces as well as stresses arising from constituent incompatibility and cohesion. In the numerical setting, evaluation of the interactive force involves a closest point projection between constituent points in the spatial configuration. Additionally, we propose a Lagrange multiplier formulation based on the method of [44] to weakly enforce the traction boundary conditions on the deformable mixture domain. This formulation implicitly determines the partial tractions carried by each constituent as a component of the total traction such that the deformation of the mixture boundary of each constituent is identical. Namely, unphysical protrusion of constituents from the mixture continuum is precluded, thereby addressing a previously unresolved issue with mixture theory.
In what follows, the finite deformation kinematics of growth in the multi-constituent context is described in Section 2. The thermodynamic balance laws are presented in Section 3. Section 4 contains the constitutive models for the scaffold and matrix as well as the evolution equations for growth. The computational realization of the theory using finite elements is developed in Section 5. Numerical results on representative volumes within a tissue are studied in Section 6. Finally, conclusions are drawn in Section 7.

2. Growing mixture kinematics

Consider a mixture consisting of \( n_c \) constituents that are designated by the superscript \( \alpha = 1, \ldots, n_c \). In the case of tissue engineering, we set \( n_c = 3 \) to represent the extracellular scaffold, the matrix of growing cells, and a fluid containing nutrients. Each constituent is assumed to occupy the same region of space \( V \subset \mathbb{R}^{n_d} \) in the material configuration for which the points in the body are parameterized by the coordinate \( X \in V \). Namely, in a homogenized sense, each physical point in \( V \) is co-occupied by a particle from each constituent [45]. These constituents undergo deformation during the elapsed time \( t \) to reach the deformed mixture volume in the spatial configuration denoted by \( v \subset \mathbb{R}^{n_d} \). For general mixtures, each constituent \( \alpha \) may deform separately from the others, and this sequence of deformations is denoted by:

\[
x = \phi^{(\alpha)} \left( X^{(\alpha)}, t \right)
\]

where \( X^{(\alpha)} \in V \) denotes the particle of constituent \( \alpha \) in the reference configuration which is mapped into the spatial point \( x \). Note that we do not invoke the assumption of vanishing relative deformations which is typical of constrained solid mixture theories [17], i.e. \( \phi^{(\alpha)} = \phi \) for all \( \alpha \), and we instead permit relative constituent interactions.

Each material point \( X \) and spatial point \( x \) are co-occupied by each constituent \( \alpha \) as a fraction of the total differential volume element, although the specific portion of the constituent within a given point may vary over time. Namely, a function \( f^{(\alpha)} \) of the collection of constituent particles may be parameterized either in the material or spatial configuration in terms of the invertible mapping \( \phi^{(\alpha)} \):

\[
f^{(\alpha)} = f^{(\alpha)}(x, t) = \tilde{f}^{(\alpha)} \left( \phi^{(\alpha)} \left( X^{(\alpha)}, t \right), t \right) = \tilde{f}^{(\alpha)} \left( X^{(\alpha)}, t \right).
\]

For the case of two constituents, Fig. 1 illustrates the concept of mapping distinct material points \( X^{(1)} \) denoted by the circle and \( X^{(2)} \) denoted by the cross into the same spatial point \( x \). Subsequently, we denote the reference configuration of particles from each constituent as \( V^{(\alpha)} \). While constituent points in the domain interior may experience relative motion, the mixture boundary and constituent boundaries are constrained to move in unison for all time (i.e. protrusion is prohibited). This constraint is enforced via a Lagrange multiplier condition described in Section 5.2. Further discussion on the construct of mapping functions in the context of mixture theory is contained in [45] and references therein.

Herein, the material and spatial gradients of a field \( f^{(\alpha)} \) are expressed as follows:

\[
\text{GRAD} \left( f^{(\alpha)} \right) = \frac{\partial \tilde{f}^{(\alpha)}}{\partial X^{(\alpha)}}, \quad \text{grad} \left( f^{(\alpha)} \right) = \frac{\partial \tilde{f}^{(\alpha)}}{\partial x}
\]

and analogous expressions hold for the material and spatial divergence operators \( \text{DIV} \left( f^{(\alpha)} \right) \) and \( \text{div} \left( f^{(\alpha)} \right) \), respectively. The material and spatial time derivatives are denoted by:

\[
\frac{D^{(\alpha)}}{Dt} \left( f^{(\alpha)} \right) = \frac{\partial}{\partial t} \left( \tilde{f}^{(\alpha)} \right) \bigg|_{X^{(\alpha)}=\text{fixed}}, \quad \frac{d}{dt} \left( f^{(\alpha)} \right) = \frac{\partial}{\partial t} \left( \tilde{f}^{(\alpha)} \right) \bigg|_{x=\text{fixed}}
\]

where the respective material or spatial coordinate is held fixed when differentiating, and the superscript indicates the particular material frame of reference.

The deformation gradient \( F^{(\alpha)} \) of constituent \( \alpha \) is defined as the material gradient of the mapping function \( \phi^{(\alpha)} \):

\[
F^{(\alpha)} = \text{GRAD} \left( \phi^{(\alpha)} \left( X^{(\alpha)}, t \right) \right), \quad f^{(\alpha)} = \det \left( F^{(\alpha)} \right) > 0.
\]
Fig. 1. Mapping of mixture constituents from material configuration (distinct neighborhoods denoted by circle and cross) to spatial configuration (overlapping neighborhood resulting from enforcing compatibility).

Similarly, the spatial velocity $v^{(\alpha)}$ is defined as the material time derivative of the deformation map:

$$v^{(\alpha)} = \frac{D^{(\alpha)}}{Dt} \phi^{(\alpha)} \left( X^{(\alpha)}, t \right). \tag{6}$$

For smooth mappings, we obtain the usual relations for the material $L^{(\alpha)}$ and spatial $l^{(\alpha)}$ gradients of the velocity field:

$$L^{(\alpha)} = \frac{D^{(\alpha)}}{Dt} F^{(\alpha)} = \text{GRAD} \, v^{(\alpha)}, \quad l^{(\alpha)} = \text{grad} \, v^{(\alpha)} = \frac{D^{(\alpha)} F^{(\alpha)}}{Dt} F^{(\alpha)-1}. \tag{7}$$

Additionally, the usual volumetric transformation formula holds for scalar-valued fields which have corresponding representations in both the material frame and spatial frame:

$$f^{(\alpha)} \left( X^{(\alpha)}, t \right) = J^{(\alpha)} f^{(\alpha)} \left( \phi^{(\alpha)} \left( X^{(\alpha)} \right), t \right), \tag{8}$$

where the subscript $\phi$ is used to denote the pull-back of a spatial quantity to the material configuration. The corresponding flux field $f^{(\alpha)}$ obeys the Piola transformation:

$$f^{(\alpha)}_{\phi} = f^{(\alpha)} f^{(\alpha)} \cdot F^{(\alpha)-T}. \tag{9}$$

Finally, relationships between the material and spatial time derivatives (4) of a field are obtained according to the chain rule and Reynold’s transport theorem as follows:

$$\frac{D^{(\alpha)}}{Dt} f^{(\alpha)} = \frac{d}{dt} f^{(\alpha)} + \text{grad} \left( f^{(\alpha)} \right) \cdot v^{(\alpha)} \tag{10}$$

$$J^{(\alpha)-1} \frac{D^{(\alpha)}}{Dt} f^{(\alpha)}_{\phi} = \frac{d}{dt} f^{(\alpha)} + \text{div} \left( f^{(\alpha)} \otimes v^{(\alpha)} \right). \tag{11}$$

2.1. Densification and volumetric growth

A distinguishing feature of mixtures is that reactions between the constituents can lead to the exchange of mass within the system and the apparent growth or decay of particular constituents. In the present generalized framework,
this interconversion is characterized both through evolution of local density and evolution of local volume. Density evolution has been the primary focus of classical mixture theory. Namely, within a fixed differential volume element of the mixture, the mass of a constituent can increase by absorbing mass from other constituents and filling in the pores of the overall volume element, leading to an apparent increase in density. Further discussion is contained in the review by Rajagopal and Tao [45]. Alternatively, the local volume of an individual constituent may increase by the laying down of additional material at a constant density. This change in volume is likely to strain the other surrounding constituents. To date, these concepts have been investigated almost exclusively using constrained mixture theory, where the deformation of all constituents is assumed to be equal such that (5) gives $F^{(α)} = F$ for all $α$. For example, Humphrey and co-workers [10,14,17] have developed mixture models for the turnover of collagen in ligaments and the growth of blood vessel walls. In the following, we briefly outline the kinematics induced by evolving density and volume, henceforth termed as density growth and volume growth.

**Remark.** Both of these classes of growth have been explored rather extensively for single-constituent materials in the context of open system mechanics. As remarked in [22], the mechanics of a growing open system can be understood with close analogy to the mechanics of an underlying mixture with one dominant constituent. The open system theory for densification is commonly applied to modeling hard biological tissue such as bone [22–25] while volume evolution is typically applied when modeling soft tissues such as blood vessels [32,33,35,46].

When describing density in the context of a mixture, clearly specifying both the configuration (spatial or material) as well as the reference volume element (mixture or constituent) is important. The current density of a constituent in the present modeling framework, this condition implies that the nutrients completely fill the pores of the overlapping scaffold and matrix constituents. We remark that (12) is not strictly imposed within the theoretical and numerical developments herein; techniques for incorporating this condition are discussed in [17,42].

The pull-back of $ρ^{(α)}$ to the material configuration is denoted by $ρ^{(α)}(X, t)$, indicating explicit dependence on position and time. The true density $ρ_R^{(α)}(X)$ of a constituent is defined with respect to its component reference frame, existing independent of the other constituents. In other words, $ρ_R^{(α)}$ denotes the density of the undeformed constituent referred to a solely-occupied volume element. All other density measures are referred to the mixture volume element which is co-occupied by all constituents. According to Mills [47], for mixtures that are void-free (implying that the constituents occupy the entire volume in the material and spatial configurations), the following additivity constraint holds:

$$\sum_{α=1}^{n_c} \frac{ρ^{(α)}}{ρ_R^{(α)}} = 1.$$  \hspace{1cm} (12)

In the present modeling framework, this condition implies that the nutrients completely fill the pores of the material configuration is denoted by $ρ^{(α)}(X, t)$, and $ρ_0^{(α)}(X^{(α)}) = ρ_φ^{(α)}(X^{(α)}, t_0) = ρ^{(α)}(x, t_0)$ is the initial density of constituent $α$ within the mixture. Notice the explicit dependence on position and time, implying that the material configuration is not entirely “stationary”. Recall that the concept of the material configuration is derived solely from deformation mappings $ϕ^{(α)}$ to ensure that the measure of the collection of material particles within the domain $ν$ remains constant with respect to the reference frame $V$. However, the state of these particles, specifically their local density and volume, is free to evolve over time according to the mixture reactions. This viewpoint closely relates to the concept of evolving natural configurations presented by Rajagopal [16,17].

Additionally, we remark that the initial density $ρ_0^{(α)}$ is related to the true density $ρ_R^{(α)}$ through the initial porosity $π_0^{(α)}(X^{(α)})$ of each constituent within the mixture:

$$ρ_0^{(α)} = π_0^{(α)} ρ_R^{(α)} , \hspace{1cm} \sum_{α=1}^{n_c} π_0^{(α)} = 1.$$  \hspace{1cm} (13)

Subsequently, quantities related to the mixture as a whole will be signified without the superscript $α$. Hence, the total mass density of the mixture is given by:

$$ρ = \sum_{α=1}^{n_c} ρ^{(α)}$$  \hspace{1cm} (14)
and the mean velocity is defined through a mass-weighted average of constituent velocities:

\[ v = \frac{1}{\rho} \sum_{\alpha} \rho_{\alpha} v_{\alpha}. \]  

(15)

Lastly, a material time derivative of field \( f^{(\alpha)} (x, t) \) with respect to the mixture velocity is defined with analogy to (10) (note the missing superscript on the differential operator \( D (\bullet) / Dt \)):

\[ \dot{f}^{(\alpha)} = \frac{D}{Dt} f^{(\alpha)} = \frac{d}{dt} f^{(\alpha)} (x, t) + \text{grad} \left[ f^{(\alpha)} (x, t) \right] \cdot v (x, t). \]  

(16)

The kinematics of growth is completed by the discussion of local volume change between the material and spatial configuration. Focusing on constituent \( \alpha \), each material particle may gain mass through a geometric change in volume. Since neighboring particles may expand or contract at different rates, the resulting configuration is likely incompatible such that further elastic straining (leading to associated stress) is required to reach an overall compatible configuration. This hypothetical sequencing of the transformations has been broadly considered in the context of open systems [32,33] and is described mathematically through a multiplicative decomposition of the deformation gradient \( F^{(\alpha)} \).

Since each constituent can gain or lose mass, we decompose each of the component mapping functions into a growth part \( F_{g}^{(\alpha)} \) and an elastic part \( F_{e}^{(\alpha)} \) as follows:

\[ F^{(\alpha)} = F_{e}^{(\alpha)} F_{g}^{(\alpha)}. \]  

(17)

This sequence of tangent maps gives rise to an intermediate configuration \( V_{g}^{(\alpha)} \) of the body, which is illustrated through Fig. 2 for the second constituent as lying between the material configuration \( V_{g}^{(\alpha)} \) and the spatial configuration \( v \). Since the decomposition (17) is applied independently at each material point, the intermediate configuration generally is not compatible [48].

All growth processes are assumed to take place during the transformation from the material to the intermediate configuration. Thus, mass is locally preserved during the purely elastic transformation between the intermediate and spatial configurations, such that the resulting expressions hold:

\[ \rho_{\phi}^{(\alpha)} = J_{g}^{(\alpha)} \rho_{g}^{(\alpha)}, \quad \rho_{g}^{(\alpha)} = J_{e}^{(\alpha)} \rho^{(\alpha)}. \]  

(18)
where $\rho_{g}^{(\alpha)}$ is the density of constituent $\alpha$ in the incompatible intermediate configuration and the Jacobian determinants emerge as:

$$J_{g}^{(\alpha)} = \det \left( F_{g}^{(\alpha)} \right), \quad J_{e}^{(\alpha)} = \det \left( F_{e}^{(\alpha)} \right). \quad (19)$$

Employing the decomposition (17) within definition (7) leads to an additive split of the spatial velocity gradient as follows:

$$l^{(\alpha)} = l_{e}^{(\alpha)} + F_{e}^{(\alpha)} l_{g}^{(\alpha)} F_{e}^{(\alpha)-1} \quad (20)$$

$$l_{e}^{(\alpha)} = \frac{D}{Dt} F_{e}^{(\alpha)} F_{e}^{(\alpha)-1}, \quad l_{g}^{(\alpha)} = \frac{D}{Dt} F_{g}^{(\alpha)} F_{g}^{(\alpha)-1}. \quad (21)$$

Lastly, we record the following expressions for the material time derivative of the constituent Jacobians [32,48]:

$$\frac{D}{Dt} l_{e}^{(\alpha)} = l_{e}^{(\alpha)} \text{tr} l^{(\alpha)}, \quad \frac{D}{Dt} l_{g}^{(\alpha)} = l_{g}^{(\alpha)} \text{tr} l^{(\alpha)} . \quad (22)$$

**Remark.** The crucial aspect for modeling density growth is the constitutive relation for evolving the material density $\rho_{\phi}^{(\alpha)}$. Similarly, various forms of volumetric growth, such as isotropic or cylindrical, are achieved by postulated evolutions of the growth mapping $F_{g}^{(\alpha)}$. Further discussion of the incompatible grown configuration $V_{g}^{(\alpha)}$ and its relationship to multiplicative decompositions employed for finite-strain plasticity are contained in [28,31].

3. Balance laws

We now record a series of balance laws that govern the deformation and evolution of the mixture. At the conclusion, we will arrive at the governing equations and a constitutive framework for the constituents of the mixture. The treatment of balance laws herein follows closely to those presented in the context of mixture theory [17,45] as well as the context of open systems [22], although specialized assumptions are applied within the balance of mixture entropy that lead to distinguishing features of the constitutive relations.

The general form of all balance laws herein is expressed through the material time derivative of a spatial volume integral. Thus, given a spatial field $A^{(\alpha)}(x,t)$ pertaining to constituent $\alpha$, its conservation over time within a fixed volume $B \subset v$ is expressed as:

$$\frac{D}{Dt} \int_{B} A^{(\alpha)} \, dv = \int_{B} \frac{dA^{(\alpha)}}{dt} \, dv + \int_{\partial B} A^{(\alpha)} v^{(\alpha)} \cdot n \, da = \int_{\partial B} A^{(\alpha)} \cdot n \, da + \int_{\partial B} A_{s}^{(\alpha)} \, dv \quad (23)$$

where $A^{(\alpha)}$ and $A_{s}^{(\alpha)}$ are respectively the associated flux and supply into constituent $\alpha$, either from external sources (e.g. applied mechanical loads) or internal sources (e.g. exchange of mass). Employing the divergence theorem and using the arbitrariness of $B$ yields the local form:

$$\frac{dA^{(\alpha)}}{dt} + \text{div} \left( A^{(\alpha)} v^{(\alpha)} \right) = \frac{D}{Dt} A^{(\alpha)} + A^{(\alpha)} \text{div} v^{(\alpha)} = \text{div} A^{(\alpha)} + A_{s}^{(\alpha)} \quad (24)$$

where (10) and the product rule of differentiation have been applied to yield the intermediate equality. Finally, applying Reynold’s transport theorem (11) to the spatial form (24) provides a corresponding balance law for the material configuration:

$$\frac{D}{Dt} A_{\phi}^{(\alpha)} \phi = \text{DIV} A_{\phi}^{(\alpha)} + A_{s,\phi}^{(\alpha)} \quad (25)$$

where the transformed supply $A_{s,\phi}$ and flux $A_{\phi}^{(\alpha)}$ fields are related to their spatial counterparts through (8) and (9), respectively.
3.1. Balance of mass

The evolution of mass between constituents is a central component of mixture theory which distinguishes it from the classical mechanics of engineered materials. Substituting the mass density $\rho^{(\alpha)}$ for $A^{(\alpha)}$ within the spatial configuration balance law (24) yields:

$$\frac{d\rho^{(\alpha)}}{dt} + \text{div} (\rho^{(\alpha)} v^{(\alpha)}) = \frac{D^{(\alpha)}}{Dt} + \rho^{(\alpha)} \text{div} (v^{(\alpha)}) = m^{(\alpha)}$$

(26)

where $m^{(\alpha)}$ is the volume specific rate of mass conversion into constituent $\alpha$ from the other constituents in the mixture. In line with traditional approaches to mixture theory [6], the contribution arising from mass fluxes between constituents has been neglected. Treatment of mass fluxes can be found in developments for open system mechanics [22,23].

The corresponding balance of mass in the material configuration is obtained from (25):

$$\frac{D^{(\alpha)}}{Dt} \rho^{(\alpha)} \phi = m^{(\alpha)} \phi.$$  

(27)

A primary tenet in the present framework is that the total mass within the mixture is conserved. Thus, by invoking (14)–(15), the summation of (26) over all constituents must vanish and the constituent mass reactions must balance:

$$\dot{\rho} + \rho \text{div} v = 0$$

(28)

$$\sum_{\alpha=1}^{n} m^{(\alpha)} = 0.$$  

(29)

To further investigate the mass balance in the present framework, we recall that the combined evolution of density and local volume (namely, growth) is restricted to the transformation from the material to the intermediate configuration according to (18). Substituting the first equality from (18) into (27) and employing (22) yields the balance of mass in the intermediate configuration:

$$J^{(\alpha)} g D^{(\alpha)} \rho^{(\alpha)} g + \rho g D^{(\alpha)} J^{(\alpha)} g = m^{(\alpha)} \phi.$$  

(30)

Within the framework of (30), each constituent within the mixture could evolve by the simultaneous change of density and volume. However, we consider herein the restricted cases of volume-preserving growth and density-preserving growth. In the first case, new material of constituent $\alpha$ is formed by increasing density while maintaining fixed local volume. Hence, the determinant of the growth deformation gradient remains constant, $J^{(\alpha)} = 1$, and its material time derivative vanishes. Substituting this simplification into (30) leads to the following:

$$m^{(\alpha)} \phi = \frac{D^{(\alpha)}}{Dt} \rho^{(\alpha)} g.$$  

(31)

This simplified expression mirrors (27) and implies that the concept of the intermediate configuration is not needed for volume-preserving growth. Thus, specifying the mass conversion rate $m^{(\alpha)} \phi$ is sufficient to close the balance of mass (27). An illustration of growth at constant volume is given in Fig. 3(a), where the scaffold and the matrix of cells are designated by black dots and white circles, respectively. Growth occurs by conversion of the nutrient fluid into the matrix solid, indicated by the enlarged circles in the lower volume element that fill in the pores of the mixture. Thus, the apparent matrix density $\rho^{(\alpha)} g$ increases while the local volume element remains constant, as denoted by the dashed lines. Motivating examples include constrained mixture theory [17,42] and densification of skeletal tissue [23].

In the second case, new material of constituent $\alpha$ is formed by expansion of the local volume at constant density. Hence, the grown configuration density is equal to the initial density of the constituent, $\rho g^{(\alpha)} = \rho^{(\alpha)}$, and its material time derivative vanishes. Combining expressions (22) and (30) leads to the following:

$$m^{(\alpha)} \phi = \frac{D^{(\alpha)} J^{(\alpha)} g \rho^{(\alpha)} g}{Dt} = J^{(\alpha)} g \rho^{(\alpha)} tr J^{(\alpha)} g.$$  

(32)
Accordingly, specifying the growth deformation gradient \( F_g^{(\alpha)} \) and its evolution is sufficient to define the mass source and close the balance equation (27). A primary example is the mechanical modeling of skin growth [32]. An illustration of growth at constant density is given in Fig. 3(b), whereby the deposition of the white matrix surrounding the black scaffold causes the expansion of the local volume element.

We remark that the validity of the assumed growth process depends upon the physical characteristics of the biological system being modeled. For example, the relative stiffness of the scaffold compared to the matrix could be an influential parameter upon the type of growth observed. Also, for each restriction (31) and (32) of the general grown density evolution (30), the constitutive model is completed by specifying the mass conversion rate. The general case of combined density and volume growth entails further complexity to develop the constitutive relations, and few attempts have been made to model such phenomena. Relevant examples are found in [41] for a computational formulation of single constituent open systems and in [43] for a theoretical formulation of cylindrical growth in mixtures.

### 3.2. Balance of linear momentum

The notion of stress within the mixture is associated with a traction vector resulting on a surface \( S \) within the spatial volume \( v \) according to Cauchy’s theorem. Since multiple constituents are present, see Fig. 1, each one may possess a traction \( t^{(\alpha)} \) that relates to a Cauchy stress \( \sigma^{(\alpha)} \) according to \( t^{(\alpha)} = \sigma^{(\alpha)} n \), where \( n \) is the unit normal on the surface \( S \). As discussed in [45], \( \sigma^{(\alpha)} \) is defined as the partial stress of constituent \( \alpha \), relating to the total Cauchy stress \( \sigma \) in the mixture at point \( x \) according to:

\[
\sigma = \sum_{\alpha=1}^{n_c} \sigma^{(\alpha)}.
\]  

(33)
These partial stresses are defined through the balance of linear momentum, obtained by substituting the momentum density $\rho^{(\alpha)} v^{(\alpha)}$ into (24):

$$\frac{d}{dt} \left( \rho^{(\alpha)} v^{(\alpha)} \right) + \text{div} \left( \rho^{(\alpha)} v^{(\alpha)} \otimes v^{(\alpha)} \right) = \text{div} \left( \sigma^{(\alpha)T} \right) + \rho^{(\alpha)} b + I^{(\alpha)} + m^{(\alpha)} v^{(\alpha)}.$$ (34)

The total momentum source is a combination of the external mechanical load $b$ (force per mass) and sources due to interactions between the constituents. The latter involves both the exchange of mass from $m^{(\alpha)}$ as well as the resultant partial force $I^{(\alpha)}$ acting on constituent $\alpha$ due to the other constituents. Note that the second-order identity tensor is denoted by $I$ without superscripts. The balance of momentum (34) will serve as the primary governing equation for each constituent within the weak formulation discussed in Section 5.

The corresponding balance law in the material configuration follows directly from (25) as:

$$\frac{D^{(\alpha)}}{Dt} \left( \rho^{(\phi)} \phi^{(\alpha)} v^{(\alpha)} \right) = \text{DIV} \left( P^{(\alpha)T} \right) + \rho^{(\phi)} \phi b + I^{(\phi)} \phi + m^{(\phi)} \phi v^{(\alpha)}.$$ (35)

where $P^{(\alpha)} = J^{(\alpha)} \sigma^{(\alpha)} F^{(a)T}$ is the first Piola–Kirchhoff stress tensor and $I^{(\phi)} = J^{(\alpha)} I^{(\alpha)}$ is the interactive force in the material configuration.

The material time derivative in (34) and (35) contains contributions both from the deformation and from evolution of density, and hence these balance laws are referred to as being volume specific, as in [22]. The mass specific counterpart is obtained from (34) by subtracting the balance of mass equation (26) weighted by the spatial velocity $v^{(\alpha)}$ and using (16) to yield:

$$\rho^{(\alpha)} \frac{D^{(\alpha)}}{Dt} v^{(\alpha)} = \text{div} \left( \sigma^{(\alpha)T} \right) + \rho^{(\alpha)} b + I^{(\alpha)}.$$ (36)

An analogous relation in the material configuration is obtained through (35) and (27):

$$\rho^{(\phi)} \frac{D^{(\phi)}}{Dt} v^{(\phi)} = \text{DIV} \left( P^{(\phi)T} \right) + \rho^{(\phi)} \phi b + I^{(\phi)}.$$ (37)

Since the momentum interactions between constituents should balance according to Newton’s third law, we have [45]:

$$\sum_{\alpha=1}^{n_c} I^{(\alpha)} + m^{(\alpha)} v^{(\alpha)} = 0.$$ (38)

Hence, summation of balances (34) over all constituents, gives the balance law for the mixture:

$$\sum_{\alpha=1}^{n_c} \left[ \frac{d\rho^{(\alpha)} v^{(\alpha)}}{dt} + \text{div} \left( \rho^{(\alpha)} v^{(\alpha)} \otimes v^{(\alpha)} \right) \right] = \text{div} \left( \sigma^{T} \right) + \rho b.$$ (39)

The interactive force $I^{(\alpha)}$ appearing in the momentum balance (34) accounts for the forces acting on constituent $\alpha$ due to relative motion with respect to the surrounding mixture, including effects such as drag, diffusion, density gradients, and differential fluid flow. Various references describing the centrality of the interactive force to mixture theory are contained in [45]. In the present solid constituent mixture, we envision the special case of a fibrous scaffold and a dispersed matrix of cells.

Consider the following physical motivation for the interactive force. Suppose that the fibers in the scaffold are initially periodically arranged. As growth of the matrix takes place, some fibers may be squeezed closer together while others may spread apart. Clearly, contact forces occur between the matrix and the scaffold to generate these deformations. However, these fibers and matrix are treated in a homogenized rather than a discrete sense within the mixture model. Thus, the differential scaffold deformation is properly characterized as a motion of the local volume of the fibers with respect to the matrix local volume. The inverse of this characterization is depicted in Fig. 1, where initially separated local volumes of the scaffold and matrix at points $X^{(\alpha)}$ are mapped into the same point $x$. This relative motion is obviously resisted by the constituents but not entirely prevented, and this motion gives rise to the interactive force that must be included in the momentum balance equation.
Note that a common assumption for modeling solid mixtures is that all of the constituents are constrained to deform concurrently \([14,17]\). In the resulting constrained mixture theory, the interactive forces vanish identically because the relative velocities between constituents are zero. These models are contained as a subset of the present framework as the special case that the deformation mappings (1) satisfy \(\phi^{(a)} = \phi\).

Remark. Observe from the momentum balance (36) that, when the stress state is homogeneous (uniform) and the acceleration is negligible, the interactive force \(I^{(a)}\) for a constituent vanishes identically. Therefore, inhomogeneous deformation and stress states are required in order to generate the interactive force. Also, the constitutive expressions for \(I^{(a)}\), such as those given in Section 4.1, should admit zero values for the cases of homogeneous stress and vanishing acceleration.

### 3.3. Balance of angular momentum

As demonstrated in [45], the balance of angular momentum for each constituent implies that the partial Cauchy stress is symmetric so long as there is vanishing angular momentum supply, which includes both external mechanical sources and interactive moments between constituents. We adopt this assumption in the present framework and therefore retain the symmetry:

\[
\sigma^{(a)} = \sigma^{(a)T}.
\]  
(40)

### 3.4. Balance of energy

Expressing the first law of thermodynamics using (24), the rate of change of each constituent’s internal and kinetic energy must balance the supplied external power as follows:

\[
\frac{d}{dt} \left( \rho^{(a)} \left[ \frac{1}{2} v^{(a)} \cdot v^{(a)} + e^{(a)} \right] \right) + \text{div} \left( \rho^{(a)} \left[ \frac{1}{2} \sigma^{(a)} \cdot v^{(a)} + \sigma^{(a)} \cdot v^{(a)} + e^{(a)} \right] \right) = \text{div} \left( \sigma^{(a)} \cdot v^{(a)} \right) + \rho^{(a)} \left( v^{(a)} \cdot b + \frac{1}{2} m^{(a)} v^{(a)} \cdot v^{(a)} + v^{(a)} \cdot I^{(a)} - \text{div} \ q^{(a)} + \rho^{(a)} r^{(a)} + m^{(a)} e^{(a)} + e^{(a)} \right)
\]  
(41)

where \(e^{(a)}\) is the specific internal energy density of the constituent, \(q^{(a)}\) is the heat flux vector, \(r^{(a)}\) is the heat source, and \(e^{(a)}\) is the energy supply. The first four terms on the right-hand side of (41) represent the mechanical external power, and the last four terms represent the non-mechanical external power. Additionally, the term \(m^{(a)} \left( \frac{1}{2} v^{(a)} \cdot v^{(a)} + e^{(a)} \right)\) accounts for the exchange of energy between constituents arising from mass transfer, and the term \(v^{(a)} \cdot I^{(a)}\) accounts for the energy due to momentum exchange. Further discussion is contained in [45].

The volume specific balance law in the material configuration corresponding the volume specific spatial balance equation (41) is obtained from (25) as:

\[
\frac{D^{(a)}}{Dt} \left( \rho^{(a)} \left[ e^{(a)} + \frac{1}{2} v^{(a)} \cdot v^{(a)} \right] \right) = \text{DIV} \left( \rho^{(a)} v^{(a)} \right) + \rho^{(a)} v^{(a)} \cdot b + \frac{1}{2} m^{(a)} v^{(a)} \cdot v^{(a)} + v^{(a)} \cdot I^{(a)} - \text{DIV} d^{(a)} + \rho^{(a)} r^{(a)} + m^{(a)} e^{(a)} + e^{(a)}
\]  
(42)

The balance of internal energy, which plays a role in the development of constitutive equations, is obtained from (41) by subtracting the balance of kinetic energy. As shown in [22], the statement of kinetic energy balance combines the mass balance equation (26) weighted by the specific kinetic energy \(K^{(a)} = \frac{1}{2} v^{(a)} \cdot v^{(a)}\) and the momentum balance equation (34) weighted by the constituent velocity \(v^{(a)}\). Combining these relations and subtracting them from (41) yields:

\[
\frac{d}{dt} \left( \rho^{(a)} e^{(a)} \right) + \text{div} \left( \rho^{(a)} e^{(a)} v^{(a)} \right) = \text{tr} \left( \sigma^{(a)} I^{(a)} \right) - \text{div} q^{(a)} + \rho^{(a)} r^{(a)} + m^{(a)} e^{(a)} + e^{(a)}
\]  
(43)

Here, the first term on the right-hand side of (43) corresponds to the mechanical internal power. Similarly, internal energy balance in the material configuration is obtained from (27), (35), and (42):

\[
\frac{D^{(a)}}{Dt} \left( \rho^{(a)} e^{(a)} \right) = \frac{D^{(a)}}{Dt} P^{(a)} - \text{DIV} q^{(a)} + \frac{1}{2} m^{(a)} v^{(a)} \cdot v^{(a)} + \rho^{(a)} r^{(a)} + m^{(a)} e^{(a)} + e^{(a)}
\]  
(44)
Finally, we assume as in [45] that the interaction energies between the constituents vanish at the mixture level:

$$\sum_{\alpha=1}^{n_c} \left[ m^{(\alpha)} e^{(\alpha)} + \frac{1}{2} m^{(\alpha)} v^{(\alpha)} \cdot v^{(\alpha)} + \eta^{(\alpha)} \cdot I^{(\alpha)} + \varepsilon^{(\alpha)} \right] = 0. \quad (45)$$

Summing over the constituents in (43) and applying (45) leads to the balance of internal energy for the mixture:

$$\sum_{\alpha=1}^{n_c} \left[ \frac{d}{dt} \left( \rho^{(\alpha)} e^{(\alpha)} \right) + \text{div} \left( \rho^{(\alpha)} e^{(\alpha)} v^{(\alpha)} \right) \right] = -\text{div} q + \rho r$$

$$+ \sum_{\alpha=1}^{n_c} \left[ \text{tr} \left( \sigma^{(\alpha)} I^{(\alpha)} \right) - \frac{1}{2} m^{(\alpha)} v^{(\alpha)} \cdot v^{(\alpha)} - v^{(\alpha)} \cdot I^{(\alpha)} \right]$$

$$\text{where the mixture heat flux and supply are } q = \sum_{\alpha=1}^{n_c} q^{(\alpha)} \text{ and } \rho r = \sum_{\alpha=1}^{n_c} \rho^{(\alpha)} r^{(\alpha)}, \text{ respectively.}$$

For completeness, we provide the mass specific balance laws obtained from (41)–(42) by applying the product rule of differentiation to the rate term on the left-hand side and incorporating the balance of mass (26)–(27):

$$\rho^{(\alpha)} \frac{D^{(\alpha)}}{D t} \left( e^{(\alpha)} + \frac{1}{2} v^{(\alpha)} \cdot v^{(\alpha)} \right) = \text{div} \left( \sigma^{(\alpha)} \cdot v^{(\alpha)} \right) + \rho^{(\alpha)} v^{(\alpha)} \cdot b + v^{(\alpha)} \cdot I^{(\alpha)} - \text{div} q^{(\alpha)}$$

$$+ \rho^{(\alpha)} r^{(\alpha)} + \varepsilon^{(\alpha)}$$

$$\rho^{(\phi)} \frac{D^{(\phi)}}{D t} \left( e^{(\phi)} + \frac{1}{2} v^{(\phi)} \cdot v^{(\phi)} \right) = \text{DIV} \left( p^{(\phi)} \cdot v^{(\phi)} \right) + \rho^{(\phi)} v^{(\phi)} \cdot b + v^{(\phi)} \cdot I^{(\phi)} - \text{DIV} q^{(\phi)}$$

$$+ \rho^{(\phi)} r^{(\phi)} + \varepsilon^{(\phi)}. \quad (47)$$

### 3.5. Balance of entropy

The second law of thermodynamics induces a directionality to the evolution of the mixture system by postulating the existence of an entropy field which has a strictly non-negative growth rate. The particular form of the second law remains a subject of debate; see relevant discussions in [42,45] regarding mixture theory and [22,32] regarding open system mechanics. Herein, we begin by adopting the balance of entropy of the mixture as a whole expressed as a summation of the balance law (24) over all constituents, which implies that the second law holds locally at each point in the mixture:

$$\frac{d}{dt} \left( \sum_{\alpha=1}^{n_c} \rho^{(\alpha)} \eta^{(\alpha)} \right) + \text{div} \left( \sum_{\alpha=1}^{n_c} \rho^{(\alpha)} \eta^{(\alpha)} v^{(\alpha)} \right) + \text{div} \left( \sum_{\alpha=1}^{n_c} q^{(\alpha)} \frac{\eta^{(\alpha)}}{\theta^{(\alpha)}} \right) - \sum_{\alpha=1}^{n_c} \rho^{(\alpha)} r^{(\alpha)} = \gamma \quad (49)$$

where $\eta^{(\alpha)}$ is the constituent specific entropy, $\theta^{(\alpha)}$ is the absolute temperature, and $\gamma \geq 0$ is the total entropy production of the mixture.

As a rational simplification, a common temperature $\theta$ is assumed across all constituents $\alpha = 1, \ldots, n_c$. Employing relation (10) for the material time derivative and substituting for the heat supply $\rho^{(\alpha)} r^{(\alpha)}$ from the balance of internal energy (43), we obtain the following:

$$\sum_{\alpha=1}^{n_c} \left[ \frac{D^{(\alpha)}}{D t} \left( \rho^{(\alpha)} \eta^{(\alpha)} + \rho^{(\alpha)} \eta^{(\alpha)} \text{div} v^{(\alpha)} \right) \right] + \sum_{\alpha=1}^{n_c} \text{div} \left( \frac{q^{(\alpha)}}{\theta} \right)$$

$$- \frac{1}{\theta} \sum_{\alpha=1}^{n_c} \left[ \frac{D^{(\alpha)}}{D t} \left( \rho^{(\alpha)} e^{(\alpha)} \right) + \rho^{(\alpha)} e^{(\alpha)} \text{div} v^{(\alpha)} \right]$$

$$+ \frac{1}{\theta} \sum_{\alpha=1}^{n_c} \left[ \text{tr} \left( \sigma^{(\alpha)} I^{(\alpha)} \right) - \text{div} q^{(\alpha)} + m^{(\alpha)} e^{(\alpha)} + \varepsilon^{(\alpha)} \right] = \gamma. \quad (50)$$
A contribution from the interactive force is incorporated into the entropy balance by recalling the mixture energy source balance assumption (45):

\[
\sum_{\alpha=1}^{n_c} \left[ \frac{D(\alpha)}{\theta} \left( \rho(\alpha) \eta(\alpha) \right) + \rho(\alpha) \eta(\alpha) \text{div} \mathbf{v}(\alpha) \right] + \sum_{\alpha=1}^{n_c} \text{div} \left( \frac{q(\alpha)}{\theta} \right) - \frac{1}{\theta} \sum_{\alpha=1}^{n_c} \left[ \frac{D(\alpha)}{\theta} \left( \rho(\alpha) e(\alpha) \right) + \rho(\alpha) e(\alpha) \text{div} \mathbf{v}(\alpha) \right] + \frac{1}{\theta} \sum_{\alpha=1}^{n_c} \left[ \text{tr} \left( \sigma(\alpha) I(\alpha) \right) - \text{div} q(\alpha) - \frac{1}{2} m(\alpha) \mathbf{v}(\alpha) \cdot \mathbf{v}(\alpha) - \mathbf{v}(\alpha) \cdot \mathbf{I}(\alpha) \right] = \gamma. \tag{51}
\]

Next, we define the specific Helmholtz free energy for each constituent as \( \psi^{(\alpha)} = e^{(\alpha)} - \theta \eta^{(\alpha)} \). Incorporating this definition into (51), multiplying through by the absolute temperature \( \theta \), using the product rule of differentiation on the entropy rate terms, and combining the terms associated with the heat flux \( q^{(\alpha)} \), we obtain the following form of entropy balance for the mixture:

\[
- \sum_{\alpha=1}^{n_c} \left[ \frac{D(\alpha)}{\theta} \left( \rho(\alpha) \psi^{(\alpha)} \right) + \rho(\alpha) \psi^{(\alpha)} \text{div} \mathbf{v}(\alpha) \right] - \sum_{\alpha=1}^{n_c} \frac{q(\alpha) \text{grad} \theta}{\theta} + \sum_{\alpha=1}^{n_c} \left[ \text{tr} \left( \sigma(\alpha) I(\alpha) \right) - \frac{1}{2} m(\alpha) \mathbf{v}(\alpha) \cdot \mathbf{v}(\alpha) - \mathbf{v}(\alpha) \cdot \mathbf{I}(\alpha) \right] - \sum_{\alpha=1}^{n_c} \left[ \rho(\alpha) \eta(\alpha) \frac{D(\alpha) \theta}{\theta} \right] = D \tag{52}
\]

where \( D = \gamma \theta \geq 0 \) is the rate of total dissipation due to thermal conversion of energy.

A mass specific form of entropy balance follows by using the product rule of differentiation and the mass balance equation (26):

\[
- \sum_{\alpha=1}^{n_c} \left[ \rho(\alpha) \frac{D(\alpha)}{\theta} \left( \psi^{(\alpha)} \right) + m(\alpha) \psi^{(\alpha)} \right] - \sum_{\alpha=1}^{n_c} \frac{q(\alpha) \text{grad} \theta}{\theta} + \sum_{\alpha=1}^{n_c} \left[ \text{tr} \left( \sigma(\alpha) I(\alpha) \right) - \frac{1}{2} m(\alpha) \mathbf{v}(\alpha) \cdot \mathbf{v}(\alpha) - \mathbf{v}(\alpha) \cdot \mathbf{I}(\alpha) \right] - \sum_{\alpha=1}^{n_c} \left[ \rho(\alpha) \eta(\alpha) \frac{D(\alpha) \theta}{\theta} \right] = D. \tag{53}
\]

We now invoke the following assumption regarding the summation of the mass flux weighted by the Helmholtz free energy:

\[
\sum_{\alpha=1}^{n_c} \left[ m(\alpha) \psi^{(\alpha)} \right] = 0. \tag{54}
\]

Neglecting this entropy term related to mass exchange between constituents will lead to a simplified form of the constitutive relations in Section 4. In general, the Helmholtz free energy is augmented by contributions from chemical energy that are consumed during the conversion of liquid and solid constituents. Hall and Rajagopal [42] show that (54) can be addressed through chemical reaction and density gradient terms within a framework of maximization of entropy production. Since the primary objective of the present developments is to investigate a numerical formulation of solid constituent mixture, the authors believe that the simplifications resulting from (54) are justified in order to maintain the clarity of the numerical approach developed in Section 5. Furthermore, we remark that the term (54) does not appear within the thermodynamic framework of open systems presented in [22] but rather is included within the entropy source term.

Substituting (54) into (53) and using the definition of the first Piola–Kirchhoff stress tensor yields:

\[
- \sum_{\alpha=1}^{n_c} \left[ \rho(\alpha) \frac{D(\alpha)}{\theta} \left( \psi^{(\alpha)} \right) \right] - \sum_{\alpha=1}^{n_c} \frac{q(\alpha) \text{grad} \theta}{\theta} + \sum_{\alpha=1}^{n_c} \left[ f^{(\alpha)} - 1 \right] p^{(\alpha)} \frac{D(\alpha)}{\theta} F^{(\alpha)} - \frac{1}{2} m(\alpha) \mathbf{v}(\alpha) \cdot \mathbf{v}(\alpha) - \mathbf{v}(\alpha) \cdot \mathbf{I}(\alpha) \right] - \sum_{\alpha=1}^{n_c} \left[ \rho(\alpha) \eta(\alpha) \frac{D(\alpha) \theta}{\theta} \right] = D. \tag{55}
\]
Now, we assume that the Helmholtz free energy of each constituent is an explicit function solely of the elastic deformation, material density, and absolute temperature as follows:

\[
\psi^{(\alpha)} = \psi^{(\alpha)} \left( F^{(\alpha)}, F^{(\alpha)}_g, \rho^{(\alpha)}, \theta \right) \equiv \tilde{\psi}^{(\alpha)} \left( F^{(\alpha)} F^{(\alpha)\!-\!1}_g, \rho^{(\alpha)}, \theta \right) = \tilde{\psi}^{(\alpha)} \left( F^{(\alpha)}_e, \rho^{(\alpha)}, \theta \right)
\]

(56)

where the elastic deformation gradient \( F^{(\alpha)}_e = F^{(\alpha)} F^{(\alpha)\!-\!1}_g \) is obtained from (17); also recall Fig. 2. As an aside, the Helmholtz function can be equivalently expressed in terms of the elastic right Green deformation tensor \( C^{(\alpha)}_e = F^{(\alpha)\!T}_e F^{(\alpha)}_e \) so long as the principle of frame invariance is satisfied [32]. Applying the material time derivative to (56) yields:

\[
\frac{D^{(\alpha)}}{Dt} \left( \psi^{(\alpha)} \right) = \frac{\partial \psi^{(\alpha)}}{\partial F^{(\alpha)}} : \frac{D^{(\alpha)} F^{(\alpha)}}{Dt} + \frac{\partial \psi^{(\alpha)}}{\partial F^{(\alpha)}_g} : \frac{D^{(\alpha)} F^{(\alpha)\!-\!1}_g}{Dt} + \frac{\partial \psi^{(\alpha)}}{\partial \rho^{(\alpha)}} \frac{D^{(\alpha)} \rho^{(\alpha)}}{Dt} + \frac{\partial \psi^{(\alpha)}}{\partial \theta} \frac{D^{(\alpha)} \theta}{Dt}
\]

\[
= \left( \frac{\partial \psi^{(\alpha)}}{\partial F^{(\alpha)}_e} \right) \left( F^{(\alpha)}_e \right) : \left( \frac{D^{(\alpha)} F^{(\alpha)}_e}{Dt} - \left( F^{(\alpha)}_g - T, F^{(\alpha)\!T}_g, F^{(\alpha)\!-\!T}_g \right) : \left( \frac{D^{(\alpha)} F^{(\alpha)\!-\!1}_g}{Dt} \right) \right) + \frac{\partial \psi^{(\alpha)}}{\partial \rho^{(\alpha)}} \frac{D^{(\alpha)} \rho^{(\alpha)}}{Dt} + \frac{\partial \psi^{(\alpha)}}{\partial \theta} \frac{D^{(\alpha)} \theta}{Dt}
\]

(57)

Incorporating (57) into (55) leads to the following Clausius–Duhem relation for the mixture dissipation:

\[
\sum_{\alpha=1}^{n_c} \left[ \left( J^{(\alpha)} - 1 \right) p^{(\alpha)} - \rho^{(\alpha)} \frac{\partial \tilde{\psi}^{(\alpha)}}{\partial F^{(\alpha)_e}} \cdot F^{(\alpha)\!-\!T}_g \right) : \frac{D^{(\alpha)} F^{(\alpha)}_e}{Dt} - \sum_{\alpha=1}^{n_c} q^{(\alpha)} \frac{\text{grad} \theta}{\theta}
\]

\[
+ \sum_{\alpha=1}^{n_c} \left[ \rho^{(\alpha)} \left( F^{(\alpha)_g - T} \cdot F^{(\alpha)\!T}_g, \frac{\partial \tilde{\psi}^{(\alpha)}}{\partial F^{(\alpha)}_e} \cdot F^{(\alpha)\!-\!T}_g \right) : \frac{D^{(\alpha)} F^{(\alpha)_e}}{Dt} \right] - \sum_{\alpha=1}^{n_c} \left[ \frac{1}{2} m^{(\alpha)} n^{(\alpha), v^{(\alpha)\!+\!v^{(\alpha)}\!+\!v^{(\alpha)}}} \cdot I^{(\alpha)} \right] - \sum_{\alpha=1}^{n_c} \left[ \left( \rho^{(\alpha)} \eta^{(\alpha)} + \rho^{(\alpha)} \frac{\partial \psi^{(\alpha)}}{\partial \rho^{(\alpha)}} \right) \frac{D^{(\alpha)} \theta}{Dt} \right] = D.
\]

(58)

We now specialize the general dissipation function (58) in preparation for the constitutive models for tissue engineering presented in Section 4, in which focus is placed on the solid constituents. These solid constituents are assumed to be hyperelastic materials; hence the dissipation term \( D \neq D \left( F^{(\alpha)_e} \right) \) does not depend upon the elastic deformation gradient. Also, the nutrient–containing fluid is assumed to deform with the mean velocity of the mixture \( v \) and to produce negligible mechanical stresses compared to the solids.

Thus, the reversibility of elastic processes implies that the first bracketed terms in (58) must vanish separately for each solid constituent, leading to constitutive relations for the first Piola–Kirchhoff stress:

\[
P^{(\alpha)} = \rho^{(\alpha)} \frac{\partial \tilde{\psi}^{(\alpha)}}{\partial F^{(\alpha)_e}} F^{(\alpha)\!-\!T}_g = \rho^{(\alpha)} P^{(\alpha)} \cdot F^{(\alpha)\!-\!T}_g, \quad P^{(\alpha)}_e = \rho^{(\alpha)} \frac{\partial \tilde{\psi}^{(\alpha)}}{\partial F^{(\alpha)_e}}
\]

(59)

where \( P^{(\alpha)}_e \) is the first Piola–Kirchhoff stress pushed forward to the intermediate configuration. Also, substituting (59) into the second bracketed term in (58) provides an expression in terms of the Mandel stress tensor in the intermediate configuration, similar to [32], which is defined as:

\[
M^{(\alpha)}_e = \left( F^{(\alpha)\!-\!T}_g \cdot F^{(\alpha)\!T}_g, \frac{\partial \tilde{\psi}^{(\alpha)}}{\partial F^{(\alpha)_e}} \cdot F^{(\alpha)\!-\!T}_g \right) : \left( F^{(\alpha)\!T}_g \right) = F^{(\alpha)\!T}_g \cdot P^{(\alpha)}_e.
\]

(60)

Finally, the entropy field is determined by:

\[
\eta^{(\alpha)} = \frac{\partial \psi^{(\alpha)}}{\partial \theta}.
\]

(61)
Table 1

Mixture framework under isothermal conditions expressed in spatial configuration.

<table>
<thead>
<tr>
<th>Equation</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance of mass</td>
<td>( \frac{d\rho^{(α)}}{dt} + \text{div} \left( \rho^{(α)} \mathbf{v}^{(α)} \right) = m^{(α)} )</td>
</tr>
<tr>
<td>Balance of linear momentum (mass specific)</td>
<td>( \rho^{(α)} \frac{Dv^{(α)}}{Dt} = \text{div} \left( \sigma^{(α)} \cdot \mathbf{v}^{(α)} \right) + \rho^{(α)} \mathbf{b} + f^{(α)} )</td>
</tr>
<tr>
<td>Balance of energy (mass specific)</td>
<td>( \rho^{(α)} \frac{Dv^{(α)}}{Dt} + \frac{1}{2} \frac{D\mathbf{v}^{(α)} \cdot \mathbf{v}^{(α)}}{m^{(α)}} = \text{div} \left( \sigma^{(α)} \cdot \mathbf{v}^{(α)} \right) + \rho^{(α)} \mathbf{v}^{(α)} \cdot \mathbf{b} + v^{(α)} \cdot f^{(α)} + e^{(α)} )</td>
</tr>
<tr>
<td>Balance of entropy (mass specific)</td>
<td>( - \sum_{α=1}^{n_c} \left[ \rho^{(α)} \frac{Dv^{(α)}}{Dt} \left( v^{(α)} \right) + m^{(α)} \psi^{(α)} \right] + \sum_{α=1}^{n_c} \left[ \frac{1}{2} m^{(α)} v^{(α)} \cdot v^{(α)} - v^{(α)} \cdot f^{(α)} \right] = D )</td>
</tr>
</tbody>
</table>

First Piola–Kirchhoff stress, Mandel stress, and intermediate configuration stress tensors

\[ p^{(α)} = p^{(α)} e^{(α)} - T, \quad M^{(α)} = M^{(α)} e^{(α)} - T, \quad p^{(α)} = p^{(α)} e^{(α)} - T, \quad p^{(α)} = p^{(α)} e^{(α)} - T \]

Reduced dissipation relation

\[ \sum_{α=1}^{n_c} \left( J^{(α)} - 1 \right) \left[ M^{(α)} : I^{(α)} - \rho^{(α)} \frac{\partial \psi^{(α)}}{\partial \rho^{(α)}} m^{(α)} \right] - \sum_{α=1}^{n_c} \left[ \frac{1}{2} m^{(α)} v^{(α)} \cdot v^{(α)} + v^{(α)} \cdot f^{(α)} \right] = D. \] (62)

Substituting (59)–(61) into (58) and employing (21) leads to the reduced dissipation relation:

\[ \sum_{α=1}^{n_c} \left( J^{(α)} - 1 \right) \left[ M^{(α)} : I^{(α)} - \rho^{(α)} \frac{\partial \psi^{(α)}}{\partial \rho^{(α)}} m^{(α)} \right] - \sum_{α=1}^{n_c} \left[ \frac{1}{2} m^{(α)} v^{(α)} \cdot v^{(α)} + \frac{v^{(α)} \cdot f^{(α)}}{\theta} \right] = D. \] (62)

This reduced dissipation relation combined with (59) serves as a framework for the mixture constitutive models in the next section. For simplicity, the mechanical and growth processes in the mixture are assumed to occur at uniform temperature such that the thermal term in (62) may be suppressed. A summary of the significant mixture equations simplified for isothermal conditions is given in Table 1.

Remark. The present developments focus upon mechanically driven growth. Other stimuli, such as biological or chemical stimuli, also influence growth of cells within tissues. Additional coupled equations governing the chemical reactions could thus be included, along with their effects on the constitutive relations. Possible contributions due to chemical reactions can be found in [42].

4. Constituent constitutive models

We now specialize the general mixture framework in the previous section to the model problem of engineered tissues. For this case, we consider three constituents: an underlying scaffold on which the cells grow, the growing mass of cells and secreted extracellular proteins collectively referred to as the matrix, and the nutrients that supply the cell growth. The constitutive models and physical aspects of each constituent are discussed in this section.

The scaffold structure is taken to represent the extracellular matrix proteins or other engineered substitutes. We envision it as a network of fibers with preferred orientation and containing various pores and open space, like a sponge. Thus, an anisotropic mechanical model is appropriate for this constituent. Also, the scaffold is assumed to be inert and does not grow over time.

The matrix of cells is treated as an isotropic material that can grow either by volume change or density change. Proposed models for the mass exchange term are inspired from the literature [23,31–33]. Comparison with experiments would be needed to determine which growth mechanism is predominant. As remarked, the relative stiffness of the scaffold likely has an effect on the predominant mode. This material is also homogeneous and considered to be present at every material point.

Finally, the nutrients are treated as a fluid which is assumed to flow with the center of mass of the mixture. The relative motion of this fluid with respect to the scaffold and matrix constituents generates small viscous drag forces. However, this interaction is inconsequential compared to the forces between the scaffold and matrix directly, and thus the fluid’s contributions to the interactive force terms are neglected. Also, the contribution of the nutrient hydrostatic
stress to the total mixture stress is neglected because their volume fraction is smaller than the scaffold and matrix and because the solid constituent stresses are more important to the overall growth process. Thus, the total number of primary constituents effectively reduces from three to two, which simplifies the finite element formulation presented in Section 6. This modeling assumption is similar to concept of open mixtures described in the context of mixture theory-based poroelasticity [13].

In summary, the preceding assumptions lead to a simplified model whereby:

- Mechanical stress develops only within the scaffold and matrix,
- Mass exchange only occurs between the matrix and nutrients,
- And interactive force only occurs between the scaffold and matrix.

Herein, the scaffold and matrix will be modeled using discrete solution fields while the equations for the nutrients will be treated implicitly. Using the mixture balance relations for mass exchange (29) and momentum exchange (38), these assumptions lead to the following relations between the mass sources and interactive forces between constituents:

\[
m^{(f)} = -m^{(m)}, \quad m^{(s)} = 0, \quad I^{(s)} = -I^{(m)}, \quad I^{(f)} \approx 0.
\]

(63)

In this equation and subsequently, the superscript \( (s) \) denotes the scaffold, \( (m) \) denotes the matrix, and \( (f) \) denotes the nutrients (fluid).

4.1. Interactive force

As discussed in Section 3.2, the modeling of the interactive force can be rather involved. Herein, three simple models are proposed: a force representing drag, a force representing incompatibility, and a force representing interface cohesion. These interactive forces can be applied either separately or in conjunction depending on the relevant physics of the mixture and nature of the constituents. A more involved expression for the dissipation term \( D \) can be obtained by considering a maximum dissipation principle, see e.g. [42].

Note that by using both of the mixture mass and momentum exchange balance laws (29) and (38), the last term in the entropy relation (62) is equivalent to:

\[
\sum_{\alpha=1}^{n_c} \left[ \frac{1}{2} m^{(\alpha)} v^{(\alpha)} \cdot v^{(\alpha)} + v^{(\alpha)} \cdot I^{(\alpha)} \right] = \sum_{\alpha=1}^{n_c} \left[ \frac{1}{2} m^{(\alpha)} u^{(\alpha)} - v^{(\alpha)} + u^{(\alpha)} \cdot I^{(\alpha)} \right]
\]

(64)

where \( u^{(\alpha)} = v^{(\alpha)} - v \) is the relative diffusion velocity with respect to the mixture mean velocity.

For our specific assumptions regarding the engineered tissue system, (64) is further simplified to obtain the following:

\[
\sum_{\alpha=1}^{n_c} \left[ \frac{1}{2} m^{(\alpha)} v^{(\alpha)} - v^{(\alpha)} + v^{(\alpha)} \cdot I^{(\alpha)} \right] = \left( v^{(m)} - v^{(s)} \right) \cdot I^{(m)}.
\]

(65)

In order to develop a drag force, the dissipation source term is taken to have the following form:

\[
D = \left( v^{(m)} - v^{(s)} \right) \cdot A \cdot \left( v^{(m)} - v^{(s)} \right) + D^{(m)}
\]

(66)

where \( A \) is a drag coefficient tensor and \( D^{(m)} \) is the dissipation due to growth in the matrix of cells, which leads to the mass exchange models in Sections 4.3 and 4.4.

Considering arbitrary relative deformations and combining (66) into (62) yields:

\[
J^{(m)} \left[ M^{(m)} \partial_{\dot{\psi}}^{(m)} m^{(m)} - \rho^{(m)} \frac{\partial \psi^{(m)}}{\partial \rho_{\phi}^{(m)}} \right] = D^{(m)}
\]

(67)

\[
I_{\text{drag}}^{(m)} = A \cdot \left( v^{(s)} - v^{(m)} \right)
\]

(68)
Thus, the drag force is proportional to the relative velocity of the constituents and vanishes when the constituents at a mixture point deform at the same velocity. The viscous drag force is motivated from the models of fluid–solid mixtures.

Additionally, the interactive force definition (68) can be expanded to include effects from incompatible relative deformations between the scaffold and matrix:

$$ I_{\text{comp}}^{(m)} = k \left[ \frac{\rho^{(m)}}{\rho J^{(s)}} p^{(s)}_e \cdot \nabla F^{(s)}_e - \frac{\rho^{(s)}}{\rho J^{(m)}} p^{(m)}_e \cdot \nabla F^{(m)}_e \right] . $$ (69)

This expression shares features with the interactive force term proposed by [42,49,50] which arises from the maximization of entropy and is motivated by the interaction of solid constituents. Notice that this force vanishes when the stress field is zero or for homogeneous deformation when the elastic deformation gradient field is spatially uniform.

Lastly, an interactive force is proposed for capturing the effect of cohesion across microscale interfaces between the scaffold and matrix constituents:

$$ I_{\text{coh}}^{(m)} (X) = k_U \left[ \phi^{(s)} (X) - \phi^{(m)} (X) \right] $$ (70)

where $k_U$ is an interfacial stiffness per unit volume. This simple relation for $I^{(m)}$ is proportional to the relative deformation of the solid constituents, representing their cross-linkages and resistance to interpenetration. Other more complicated relationships could also be considered.

### 4.2. Scaffold constituent

Presently, the scaffold is understood as the underlying strands of engineered material on which the cells grow. Therefore, this constituent is inert and does not experience growth, which simplifies its constitutive model. Assuming a uni-directional fiber network, we adopt the following expression for the homogenized Helmholtz free energy:

$$ \psi^{(s)} = \frac{1}{\rho^{(s)}} \pi^{(s)}_0 \psi_S , \quad P^{(s)} = \frac{\rho^{(s)}}{\rho^{(s)}} \pi^{(s)}_0 \frac{\partial \psi_S}{\partial F^{(s)}} = \pi^{(s)}_0 \frac{\partial \psi_S}{\partial F^{(s)}} $$ (71)

$$ \psi_S (F) = \beta \psi_M (F) + \frac{1}{4} E_S [(F \cdot m) \cdot (F \cdot m) - 1]^2 $$ (72)

$$ \psi_M (F) = \frac{1}{2} \mu_M (F : F - 3 - 2 \ln J) + \frac{1}{2} \lambda_M (\ln J)^2 . $$ (73)

The material parameters in (72) are: the Young’s modulus of the fibers $E_S$, fiber orientation unit vector $m$, and Lame parameters of the matrix $\mu_M$, $\lambda_M$. A fraction of the matrix stiffness is included to account for the initial transverse stiffness between the fibers before growth takes place; effectively, the parameter $\beta$ represents a portion of the matrix that is closely bound to the scaffold which does not participate in the growth processes. Therefore, $E_S$ corresponds to the Young’s modulus of the fibers in the scaffold that could be experimentally measured in a uni-axial tension test.

The stress tensor for the scaffold results from substituting (72) into (59):

$$ P^{(s)} (F) = \pi^{(s)}_0 \frac{\partial \psi_S}{\partial F} = \pi^{(s)}_0 [\beta P_M (F) + E_S [(F \cdot m) \cdot (F \cdot m) - 1] [(F \cdot m) \otimes m]] $$ (74)

$$ P_M (F) = \frac{\partial \psi_M}{\partial F} = \mu_M \left[ F - F^{-T} \right] + \lambda_M (\ln J) F^{-T} . $$ (75)

Expressions for the acoustic material moduli, appearing in the consistent tangent matrix of the numerical formulation, are contained in the Appendix.

Before proceeding to the discussion of the matrix, we provide a thought experiment to motivate the inclusion of the initial porosity $\pi^{(s)}_0$ in the material model (71). Consider a mixture consisting entirely of the scaffold but split into two constituents such that each free energy function is given by (71). Let the initial porosity of the two constituents
be \( \pi_0^{(1)} = 0.6 \) and \( \pi_0^{(2)} = 0.4 \). Since both are the same material, the deformation of each constituent is expected to be identical, \( F^{(1)}(X^{(1)}) = F^{(2)}(X^{(2)}) \). Hence, the total mixture stress follows from (12) and (33) as:

\[
P = \sum_{\alpha=1}^{2} P^{(\alpha)} = \sum_{\alpha=1}^{2} \frac{\rho_0^{(\alpha)} \partial \psi^{(\alpha)}}{\partial F^{(\alpha)}} = \sum_{\alpha=1}^{2} \frac{\partial \left( \rho_0^{(\alpha)} - 1 \psi^{(\alpha)} \right)}{\partial F^{(\alpha)}} = \sum_{\alpha=1}^{2} \frac{\partial \psi^{(\alpha)}}{\partial F} = \frac{\partial \psi^{(\alpha)}}{\partial F}.
\]

This result (76) corresponds exactly to the classical definition of a homogeneous hyperelastic material that does not experience growth. Thus, we recover the classical closed system mechanics of a single constituent from the mixture framework of Section 4 when all constituents are identical, which is logical. Also, the result shows the importance of using the initial porosity inside the Helmholtz free energy of the constituent, so that the classical form can be used for the mechanical part, and that the material properties contained in the model correspond to the properties of the material existing alone outside the mixture.

### 4.3. Matrix constituent: density growth model

We first treat the case of a stiff scaffold that permits growth of the matrix only by densification. The kinematics was described in Sections 2.1 and 3.1. Accordingly, the distinction of the intermediate configuration vanishes in this context:

\[
F^{(m)} = 1, \quad F^{(m)} = F^{(m)}, \quad \frac{\partial F^{(m)}}{\partial t} = 0.
\]

The evolution of density is prescribed through a mass conversion rate driven by the mechanical energy or Helmholtz free energy. The functional form is inspired by the work of Kuhl et al. [23] which was applied to model the growth of skeletal tissue:

\[
m^{(m)} = k_\rho \left[ \left( \frac{\rho_0^{(m)}}{\rho_0^{(m)}} \right)^{m_\rho} \rho_\phi^{(m)} \psi^{(m)} - \psi^{(m)} \right]
\]

where \( \psi^{(m)}_* \) is a baseline energy level at which the constituent density is stationary, the exponent \( m_\rho \) controls the rate of the density evolution, and \( k_\rho \) is a dimensional-consistency parameter with units of time divided by length squared. Herein, \( k_\rho \) is taken as unity, while other models for anisotropic growth have employed density-dependent functions [21,51]. Model (78) neglects the so-called dead zone or lazy zone, which is supported by recent evidence [52].

The matrix is treated as an isotropic material that grows around the fibers and fills in the mixture pores. Thus, its Helmholtz free energy is taken as follows, in terms of the initial porosity and a weighted density fraction:

\[
\psi^{(m)} = \psi^{(m)}(F^{(m)}, \rho_\phi^{(m)}) = \left( \frac{\rho_\phi^{(m)}}{\rho_0^{(m)}} \right)^{n_\rho} \frac{1}{\rho_\phi^{(m)}} \pi_0^{(m)} \psi_M(F^{(m)})
\]

where \( \psi_M \) is defined in (73) and the exponent \( n_\rho \) relates to the porosity of the material, with values between 1.0 and 3.5 [23,50].

The stress tensor follows from (59) and (79) (see also (75)):

\[
P^{(m)} = \pi_0^{(m)} \left( \frac{\rho_\phi^{(m)}}{\rho_0^{(m)}} \right)^{n_\rho} \frac{\partial \psi_M}{\partial F^{(m)}}.
\]

Substituting (77)–(80) into the reduced inequality (67) provides an expression for the dissipation:

\[
\mathcal{D}^{(m)} = J^{(m)^{-1}} (1 - n_\rho) k_\rho \left[ \left( \frac{\rho_\phi^{(m)}}{\rho_0^{(m)}} \right)^{m_\rho} \rho_\phi^{(m)} \psi^{(m)} - \psi^{(m)}_* \right] \psi^{(m)}.
\]
Within the numerical formulation of Section 5, the density evolution (78) and stress tensor (80) are solved in a coupled manner at material points corresponding to the numerical quadrature points. Implicit backward Euler time discretization is applied to the rate equation, and the nonlinear equation is solved using a scheme proposed in [23]; relevant steps are summarized in the Appendix.

4.4. Matrix constituent: volume growth model

As a second option for growth, we consider a cylindrical growth model to represent volumetric growth of the matrix. This case corresponds to a softer scaffold that does not restrict volumetric expansion or increasing the spaces between the fibers, such as in Fig. 3(b). Since the cells fill in the gaps between the fibers, we consider radial expansion or deposition around the scaffold fibers rather than isotropic growth [43]. The cylindrical growth deformation is expressed in terms of a radial growth stretch ratio

\[
m^{(m)}_{\phi} = 2\nu \frac{D^{(m)}\nu}{Dt} \rho_{0}^{(m)}, \quad \rho_{\phi}^{(m)} = \nu^2 \rho_{0}^{(m)}.
\]

(83)

The evolution of the radial stretch \(\nu\) is assumed to be driven by the components of the Mandel stress tensor \(M_{e}^{(m)}\) in the transverse plane:

\[
\frac{D^{(m)}\nu}{Dt} = k(\nu) \left[ \text{tr} \left( M_{e}^{(m)} \right) - m \cdot M_{e}^{(m)} \cdot m \right].
\]

(84)

This growth evolution rule is adapted from a model proposed in [33] for arterial wall growth, where the Mandel stress (equivalent to the negative of the quasi-static Eshelby stress [36]) is recommended as the driving mechanism rather than the second Piola–Kirchhoff stress as was adopted in [31].

The rate parameter \(k(\nu)\) is represented via a power-law to preclude unlimited growth:

\[
k(\nu) = k_+ \left[ \frac{\nu^+ - \nu^-}{\nu^+ - 1} \right]^{m_+} \quad \text{if} \quad \left[ \text{tr} \left( M_{e}^{(m)} \right) - m \cdot M_{e}^{(m)} \cdot m \right] > 0
\]

\[
k(\nu) = k_- \left[ \frac{\nu^- - \nu^+}{1 - \nu^-} \right]^{m_-} \quad \text{if} \quad \left[ \text{tr} \left( M_{e}^{(m)} \right) - m \cdot M_{e}^{(m)} \cdot m \right] < 0.
\]

(85)

In this manner, different limiting stretch ratios \(\nu^{(\beta)}\), baseline growth rate \(k^{(\beta)}\), and exponent \(m^{(\beta)}\) may be specified for tension or compression (\(\beta = +/–\)). Observe that \(k^{(\beta)}\) represents the rate of initial growth when \(\nu = 1\) and \(m^{(\beta)}\) controls how rapidly this rate decays to zero as \(\nu \rightarrow \nu^{(\beta)}\).

Remark. The growth model (82)–(85) possesses two limitations for capturing observed physiological response. First, soft tissues such as arteries typically exist in a natural pretensioned state at which growth does not occur. Perturbations about this homeostatic stress lead to growth which returns the internal stress to a similar level [53]. The current form of (84) lacks this non-zero homeostatic stress. Second, several health issues are associated with unbounded or unstable volumetric growth, such as vascular aneurysms. These two limitations are rectified by more advanced models for normal and abnormal vascular tissues [14,37–39]. Recent studies [54,55] have shown that these models ensure limited growth under arbitrary perturbations for a sufficient mechanosensitivity but allow unlimited growth and remodeling otherwise. Such constitutive models could also be accommodated within the proposed generalized mixture framework.
The Helmholtz free energy for the matrix experiencing volumetric growth is taken as:

\[
\psi^{(m)}(F_e^{(m)}, \rho_{\phi}^{(m)}) = \frac{1}{\rho_{\phi}^{(m)}\rho_0^{(m)}} \psi_M\left(F_e^{(m)}\right).
\]  

(86)

And thus the first Piola–Kirchhoff stress in the intermediate configuration follows from (59):

\[
P_e^{(m)} = \rho_0^{(m)} \frac{\partial \psi_M}{\partial F_e^{(m)}}.
\]  

(87)

Substituting (83)–(87) into the reduced inequality (67) becomes, after some manipulations:

\[
D^{(m)} = J^{(m)-1} \left[ \text{tr} \left( M_e^{(m)} \right) - m \cdot M_e^{(m)} \cdot m \right] \frac{k(\nu)}{\nu} \left[ \text{tr} \left( M_e^{(m)} \right) - m \cdot M_e^{(m)} \cdot m + \pi_0^{(m)} \psi_M \right]
\]

(88)

where the Mandel stress is given in (60). The stress tensor \( P_e^{(m)} \) and growth stretch ratio \( \nu \) are evolved using an algorithm analogous to the one for isotropic volumetric growth proposed in [33]. Relevant expressions are provided in the Appendix.

**Remark.** We wish to highlight that the volumetric growth model leads to fundamentally different material response than the density growth model in the context of mixture theory. Consider a cube of scaffold and matrix constituents free from external forces. If the matrix density evolves according to (78), the size of the cube will remain unchanged, and therefore neither the matrix nor scaffold will experience an internal stress. However, if the matrix growth deformation gradient \( F_e^{(m)} \) evolves according to (82), this deformation will not be locally compatible with the matrix, and in general each constituent will experience an internal stress generated from the elastic deformation required to restore mixture compatibility. The reader should be aware of this subtle difference in constitutive models when attempting to model particular tissue phenomena.

### 5. Weak formulation of mixture framework

With the balance laws from Section 3 and the constitutive models from Section 4, we now present the initial boundary value problem associated with the tissue mixture and the corresponding proposed numerical method for solving the problem. We restrict our discussions to the isothermal case (see Table 1). The governing equations are the momentum balance equation (37) for each constituent and the density evolution of the matrix (30), which are expressed in the material configuration. These equations are posed over the time interval \([0, T]\) and over the constituent volumes \( V^{(s)} \) and \( V^{(m)} \) which occupy the same space in the material configuration:

\[
\rho^{(s)} \frac{D^{(s)} V^{(s)}}{dt} = \text{DIV} \left( P^{(s)} T \right) + \rho^{(s)} b + I^{(s)}_{\phi} \quad \text{in} \ V^{(s)} \times \ ]0,T[.
\]

(89)

\[
\rho^{(m)} \frac{D^{(m)} V^{(m)}}{dt} = \text{DIV} \left( P^{(m)} T \right) + \rho^{(m)} b + I^{(m)}_{\phi} \quad \text{in} \ V^{(m)} \times \ ]0,T[.
\]

(90)

\[
J^{(m)} \frac{D^{(m)} M^{(m)}}{Dt} + \rho^{(m)} \frac{D^{(m)} J^{(m)}}{Dt} = \dot{m}^{(m)} \quad \text{in} \ V^{(m)} \times \ ]0,T[.
\]

(91)

\[
\phi^{(s)} = \phi^{(m)} = \bar{\phi} \quad \text{on} \ \partial V \times \ ]0,T[.
\]

(92)

\[
\phi^{(s)} \left( X^{(s)}, 0 \right) = X^{(s)} \quad \text{in} \ V^{(s)}, \quad \phi^{(m)} \left( X^{(m)}, 0 \right) = X^{(m)} \quad \text{in} \ V^{(m)}
\]

(93)

\[
\rho^{(s)} \left( X^{(s)}, 0 \right) = \rho_0^{(s)} \quad \text{in} \ V^{(s)}, \quad \rho^{(m)} \left( X^{(m)}, 0 \right) = \rho_0^{(m)} \quad \text{in} \ V^{(m)}.
\]

(94)

Expressions for the constituent stress tensors \( P^{(a)} \) and the interactive force \( I^{(a)}_{\phi} \) are found in Section 4. The mass balance relation (91) may be evaluated from (77), (78) or (82), (83) depending on whether density growth or volume
growth, respectively, is considered for the matrix. Dirichlet conditions (92) are prescribed along the entire domain boundary \( \partial V \) in order to simplify the developments that follow. The generalization to Neumann boundary conditions is non-trivial for mixture theory and is discussed further in the next section.

The time-continuous weak form corresponding to the momentum balance equations (89)–(90) is obtained by multiplying by a weighting function \( w^{(s)}(\alpha) \), integrating over the domain, and applying integration by parts.

\[
\int_{V^{(s)}} w^{(s)}(\phi) \cdot \rho^{(s)}(\phi) \frac{D^{(s)} v^{(s)}}{Dt} \, dV + \int_{V^{(s)}} \nabla w^{(s)}(\phi) : \mathbf{p}^{(s)} \, dV - \int_{V^{(s)}} w^{(s)}(\phi) \cdot \mathbf{I}^{(s)} \, dV \\
= \int_{V^{(s)}} w^{(s)}(\phi) \cdot \rho^{(s)}(\phi) \mathbf{b} \, dV
\]

\[
\int_{V^{(m)}} w^{(m)}(\phi) \cdot \rho^{(m)} \frac{D^{(m)} v^{(m)}}{Dt} \, dV + \int_{V^{(m)}} \nabla w^{(m)}(\phi) : \mathbf{p}^{(m)} \, dV - \int_{V^{(m)}} w^{(m)}(\phi) \cdot \mathbf{I}^{(m)} \, dV \\
= \int_{V^{(m)}} w^{(m)}(\phi) \cdot \rho^{(m)} \mathbf{b} \, dV. \tag{95}
\]

Notice that the density evolution (91) is an ordinary differential equation in time. Therefore, it will be treated implicitly as an internal state variable equation such that the matrix stress \( \mathbf{p}^{(m)} \) can be evaluated by a stress update procedure analogous to open system mechanics [23,33] and elastoplasticity [56]. Additionally, the constituent momentum equations (95)–(96) are coupled through the interactive force term.

We observe that typical growth rates of biological tissues operate on a time scale much longer than the material natural frequencies and the transient load effects. Also, we assume herein that the external loads and changes to the boundary conditions are applied very slowly. Therefore, the inertial effects of the constituents are neglected in the subsequent developments. For situations with rapidly varying loads and induced transient response, the concepts from two-scale temporal formulations could be adapted from [14].

Hence, each nonlinear equation is treated in a quasi-static manner and is discretized in time using the implicit backward Euler method. An incremental solution strategy is employed with a fixed time step size \( \Delta t \). The resulting mixture equations at an instant \( t_{n+1} \in [0, T] \) in time are given by:

\[
\int_{V^{(s)}} \nabla w^{(s)}(\phi) : \mathbf{p}^{(s)}_{n+1} \, dV - \int_{V^{(s)}} w^{(s)}(\phi) \cdot \mathbf{I}^{(s)}_{n+1} \, dV = \int_{V^{(s)}} w^{(s)}(\phi) \cdot \rho^{(s)}_{n+1} \mathbf{b}_{n+1} \, dV \tag{97}
\]

\[
\int_{V^{(m)}} \nabla w^{(m)}(\phi) : \mathbf{p}^{(m)}_{n+1} \, dV - \int_{V^{(m)}} w^{(m)}(\phi) \cdot \mathbf{I}^{(m)}_{n+1} \, dV = \int_{V^{(m)}} w^{(m)}(\phi) \cdot \rho^{(m)}_{n+1} \mathbf{b}_{n+1} \, dV. \tag{98}
\]

For our numerical approximation, each constituent equation is spatially discretized into a series of finite elements that cover the domain \( V^{(\alpha)} \). In the material configuration, the finite element meshes coincide, meaning that each node of the scaffold mesh has a corresponding node in the matrix mesh; see Fig. 4(a). The evolution of the constituent volume \( V^{(\alpha)} \) is obtained from the Lagrangian perspective by tracking the nodal values of the deformation field \( \phi^{(\alpha)} \).

Note that each constituent can deform independently, in contrast to constrained mixture formulations. Nonetheless, internal force term and external force term in (97) and (98) each contain contributions solely from one constituent. Therefore, these domain integrals may be evaluated by the usual finite element assembly procedure, which may be recycled from implementations for classical engineering materials with no modifications. Only the interactive force terms, which involve contributions from both constituents, require special treatment, as discussed in Section 5.1. This simplified algorithmic treatment is a key feature of the proposed mixture formulation.

**Remark.** Recall from Section 2 that the interactive force is defined for co-located points in the spatial configuration from each constituent mapping according to (1). This modeling context is more general and can readily be extended to the interaction of solid–fluid constituents, in contrast to interactive force models referenced to the constituents’ material configuration such as in [49].

As a concrete example, consider a two dimensional domain for the matrix constituent discretized with four node bilinear quadrilateral elements denoted by \( \Omega^{(m)} \). Adopting a four point Gauss quadrature rule to evaluate the integral
expressions, the first term in (98) is evaluated through an assembly over all elements as follows:

$$\sum_e \left\{ \int_{\Omega_e^{(m)}} \text{GRAD} w_{\phi}^{(m)} : P_n^{(m)} \, dV \right\} \approx \sum_e \left\{ \sum_{i=1}^{4} \left[ \text{GRAD} w_{\phi}^{(m)} \left( X_i^{(m)} \right) : P_n^{(m)} \left( X_i^{(m)} \right) \right] \right\} \left(99\right)$$

where $X_i^{(m)}$ is the location of quadrature point $i$ in element $\Omega_e^{(m)}$ and $w_i$ and $j_i$ are the quadrature weight and determinant of the elemental Jacobian, respectively. Similarly, the scaffold constituent is evaluated by a separate assembly operation employing the same quadrature rule. Since each constituent has a distinct deformation field $\phi^{(s)}$, the spatial configuration on the domain interior of each constituent may be different. However, the assembly operation for one constituent is entirely distinct from the other, as can be seen from (99). Only the interactive force terms require special treatment through a projection operation described in Section 5.1.

An outline of the computational procedure for the mixture containing two constituents is presented in Table 2. The mixture system of nonlinear equations is solved using a monolithic Newton–Raphson scheme; staggered schemes could also be devised. For the inert scaffold constituent, the stress and density follow directly by evaluating the hyperelastic relation (71) and the classical density relation $\rho^{(s)} = J^{(s)} - 1 \rho_0^{(s)}$. The matrix stress and corresponding internal variable (density or stretch ratio) are evaluated through a return mapping algorithm at the integration points of its finite element mesh. These algorithms are summarized in the Appendix. For both constituents, we employ the classical architecture of finite element codes containing element subroutines and material integration modules. In
essence, the mixture domain contains twice the number of elements and nodes compared to a single constituent, and assembly is performed progressively from the first scaffold element to the last matrix element.

Remark. A key feature of the present framework in contrast to constrained mixture theory is that the local incompatibility between constituents within the microstructure can be resolved. This generalized theory is numerically realized for the first time for solid mixtures by employing separate deformation field interpolations for each constituent. Additionally, by considering growth to occur only within the matrix constituent, the degree of anisotropy observed from the mixture can evolve while the scaffold constituent remains inert over time.

5.1. Closest point projection for interactive force

While the internal forces and external forces in each constituent can be evaluated independently on each constituent finite element mesh, the interactive force terms in (97) and (98) involve contributions from each constituent. Our treatment of these terms shares striking similarity to the closest point projection algorithms employed for the computational contact mechanics of deformable bodies; see [57] and references therein. Here, we consider the treatment of the drag force in the matrix according to (68); the treatment of the interactive force on the scaffold computational contact mechanics of deformable bodies; see [57] and references therein. Here, we consider the treatment of these terms shares striking similarity to the closest point projection algorithms employed for the finite element mesh, the interactive force terms in (97) and (98) involve contributions from each constituent. Our assembly is performed progressively from the first scaffold element to the last matrix element.

Table 2
Mixture finite element algorithm.

For each time step \( n \):
1. Assembly over scaffold elements \( \Omega_e^{(s)} \)
   1.a. Internal force: \( \sum_e \int_{\Omega_e^{(s)}} \text{GRAD} w_\phi^{(s)} : \rho_n^{(s)} dV \)
   1.b. Interactive force: Compute projection from scaffold onto matrix according to Section 5.1
2. Assembly over matrix elements \( \Omega_e^{(m)} \)
   2.a. Internal force and internal variable update:
       Update interval variable \( \rho_y \) or \( v \) according to Appendix
       Evaluate \( \sum_e \int_{\Omega_e^{(m)}} \text{GRAD} w_\phi^{(m)} : \rho_n^{(m)} dV \)
   2.b. Interactive force: Compute projection from matrix onto scaffold according to Section 5.1
3. Perform Newton–Raphson update for mixture:
   3.a. Evaluate residual \( R^{(\alpha)} = F^{(\alpha)}_{\text{external}} - F^{(\alpha)}_{\text{stress}} - F^{(\alpha)}_{\text{interact.}} \)
   3.b. If \( \| R^{(\alpha)} \| < \epsilon \) record \( d^{(s)} \), \( d^{(m)} \) and set \( n \rightarrow n + 1 \); Exit.
   3.c. Solve:
       \[
       \begin{bmatrix}
         K^{(s)} & K^{(sm)} \\
         K^{(ms)} & K^{(m)}
       \end{bmatrix}
       \begin{bmatrix}
         \Delta d^{(s)} \\
         \Delta d^{(m)}
       \end{bmatrix}
       =
       \begin{bmatrix}
         R^{(s)} \\
         R^{(m)}
       \end{bmatrix}
       \]
   3.d. Update: \( d^{(\alpha)} = d^{(\alpha)} + \Delta d^{(\alpha)} \); Return to phase 1.
the velocity field as well as any internal variables is conveniently expressed through their values at the Gauss points of the scaffold constituent:

$$
\sum_{c} \left\{ \int_{Q_{c}^{(s)}} w_{\phi}^{(m)} \cdot A \cdot v^{(s)} \, \text{d}V \right\} \approx \sum_{c} \left\{ \sum_{i=1}^{4} \left[ w_{\phi}^{(m)} \left( X_{i}^{(s)} \right) \cdot A \cdot v^{(s)} \left( X_{i}^{(s)} \right) w_{i} \phi \right] \right\}.
$$

(102)

To evaluate the weighting function, we adopt a coordinate projection algorithm similar to contact mechanics. Recall that the equilibrium of the mixture is resolved in the spatial configuration. While the integrals have been transformed to $X$ points, i.e.

$$
X_{i} = w_{\phi}^{(m)} \left( X_{i}^{(m)} \right) = \phi^{(m)-1} \left( x^{(m)} \right) = X^{(m)}.
$$

Due to the relative deformation of the constituents, these spatial points may not correspond to coinciding material points, i.e. $X^{(s)} = \phi^{(s)-1} \left( x^{(s)} \right) \neq \phi^{(m)-1} \left( x^{(m)} \right) = X^{(m)}$. See also Fig. 1. Thus, evaluating the weighting function involves a projection through the two mapping functions of the constituents:

$$
\left. w_{\phi}^{(m)} \left( X^{(m)} \right) \right|_{X^{(s)}} = w_{\phi}^{(m)} \left( \phi^{(m)-1} \left( X^{(s)} \right) \right) = w_{\phi}^{(m)} \left( \phi^{(m)-1} \left( X^{(s)} \right) \phi^{(m)-1} \left( X^{(s)} \right) \right).
$$

(103)

This projection is illustrated through the material and spatial configurations in Fig. 4(c), where the quadrature point in the scaffold denoted by the symbol “×” is used to locate the corresponding mapped point in the matrix denoted by the circle “o”. The operation involves a search for the element in the matrix that is closest to the scaffold point $X_{i}^{(s)}$. Details for evaluating this search in terms of elemental parametric coordinates and shape functions can be found in [57]. Typically, the relative deformation of the constituents is small enough such that this projection does not lie outside of the original overlapping element in the initial configuration. In case the mapped point does lie outside, a search algorithm is employed amongst the neighboring elements. This projection process is repeated with reversed roles for evaluating the interactive force in the scaffold, $F_{n+1}^{(s)}$.

To evaluate the velocity field $v^{(s)}$ in the drag-type force (68), a finite difference formula is applied to the deformation field using the time step $\Delta t$:

$$
v_{n+1}^{(s)} = \left( \frac{\phi_{n+1}^{(s)} - \phi_{n}^{(s)}}{\Delta t} \right).
$$

(104)

Within the incompatibility-type force (69), the gradient of the elastic deformation gradient $\nabla F_{e}^{(s)}$ needs to be evaluated. For finite element interpolations with linear polynomial functions, the second derivative field vanishes identically. In order to approximate this term, an elemental projection is performed using a least-squares fit of $F_{e}^{(s)}$ across all integration points within an element, and a constant value of the derivative field is obtained. This approach was successfully applied for a gradient-based formulation of crystal plasticity involving geometrically-necessary dislocations [58,59]. Details of the component-wise projection of the tensor field within an element are provided in these references.

Remark. The above approach is a mechanics-based approach for approximating the $\nabla F_{e}^{(s)}$ term. A mathematical approach would involve the use of quadratic shape functions along with evaluation of consistent second derivatives [60].

Remark. The consistent linearization of the closest-point projection (103) gives rise to higher order terms involving the shape function parametric coordinates, analogous to those obtained for finite strain contact mechanics. Due to the small relative deformations of the constituents observed in the examples, we have chosen not to implement these terms within the tangent matrix of the Newton–Raphson method. Satisfactory convergence rates were obtained by using only the first order terms, namely those obtained by linearizing (100) with the assumption $X_{i}^{(s)} \approx X_{i}^{(m)}$.

5.2. Lagrange multiplier method for tying exposed constituent boundaries

The weak form (95) is appropriate for simulating a composite domain for which the entire boundary is prescribed with Dirichlet boundary conditions. However, when portions of the boundary of $\Omega$ are considered to be traction free, the current theory does not impose a relationship between the deformations of individual constituent domain boundaries with respect to the mixture domain boundary, even though the initial configurations are coincident.

While the relative motion of the specimens would be penalized by the interactive force terms within the interior of the domain and approaching to the domain boundary, the boundaries of the overlapping constituent domains are...
where the key idea is that the governing equations (89)–(90) are supplemented by the following boundary conditions on the free surface \( \Gamma_\sigma \subset \partial V^{(\alpha)} \):

\[
\begin{align*}
P^{(s)} N^{(s)} + \lambda^{(s)} &= 0 \quad \text{on} \Gamma_\sigma, & \quad P^{(m)} N^{(m)} + \lambda^{(m)} &= 0 \quad \text{on} \Gamma_\sigma \\
\phi^{(s)} - \varphi = 0 \quad \text{on} \Gamma_\sigma, & \quad \phi^{(m)} - \varphi = 0 \quad \text{on} \Gamma_\sigma \\
\bar{T} + \lambda^{(s)} + \lambda^{(m)} &= 0 \quad \text{on} \Gamma_\sigma
\end{align*}
\]

(105)

(106)

(107)

where \( N^{(\alpha)} \) is the unit outward normal to the constituent domain \( V^{(\alpha)} \). The Lagrange multipliers \( \lambda^{(\alpha)} \) represent the value of the partial traction on surface \( \Gamma_\sigma \) derived from constituent \( \alpha \), and the trace field \( \varphi \) represents the common value of the mixture deformation mapping and the individual constituents along \( \Gamma_\sigma \). Recall that the combined mixture traction is defined by \( P N = P^{(s)} N^{(s)} + P^{(m)} N^{(m)} \) according to (33). The prescribed value of the traction externally applied to the mixture is denoted by \( \bar{T} \), which is zero for a free surface. The weak constraints provided by (105)–(107) enable the imposition of nonzero tractions, representing the measured forces applied to the composite mixture, while still enforcing that the deformation of the constituents at the boundary remain compatible.

**Remark.** Note that the minimum required constraint is that the normal component of the displacements remains compatible; in fact, the in-plane components at the surface could be distinct in order to capture shearing incompatibilities. These levels of constraint depend on the physical bonding of the constituents along the domain surface. In order to simplify the formulation, we propose to tie all components of the displacement field together rather than simply the normal component. A more general treatment could be pursued in subsequent work. Also, we remark that imposing the constraints (105)–(107) in the material configuration removes the ambiguity of defining the unit normal of the composite mixture with respect to the constituents.

The mixed weak form incorporating (97)–(98) along with (105)–(107) involves the simultaneous solution for \( \phi^{(s)}, \phi^{(m)}, \lambda^{(s)}, \lambda^{(m)}, \) and \( \varphi \):

\[
\begin{align*}
\int_{V^{(s)}} \text{GRAD} w^{(s)}_\phi : P^{(s)}_{n+1} \, dV - \int_{V^{(s)}} w^{(s)}_\phi \cdot I^{(s)}_{n+1} \, dV + \int_{\Gamma_\sigma} w^{(s)}_\phi \cdot \lambda^{(s)} \, d\Gamma \\
= \int_{V^{(s)}} w^{(s)}_\phi \cdot b_{n+1} \, dV
\end{align*}
\]

(108)

\[
\begin{align*}
\int_{V^{(m)}} \text{GRAD} w^{(m)}_\phi : P^{(m)}_{n+1} \, dV - \int_{V^{(m)}} w^{(m)}_\phi \cdot I^{(m)}_{n+1} \, dV + \int_{\Gamma_\sigma} w^{(m)}_\phi \cdot \lambda^{(m)} \, d\Gamma \\
= \int_{V^{(m)}} w^{(m)}_\phi \cdot b_{n+1} \, dV
\end{align*}
\]

(109)

\[
\begin{align*}
\int_{\Gamma_\sigma} \mu^{(s)} \cdot (\phi^{(s)} - \varphi) \, d\Gamma = 0, & \quad \int_{\Gamma_\sigma} \mu^{(m)} \cdot (\phi^{(m)} - \varphi) \, d\Gamma = 0 \\
\int_{\Gamma_\sigma} \psi \cdot (\bar{T} + \lambda^{(s)} + \lambda^{(m)}) \, d\Gamma = 0
\end{align*}
\]

(110)

(111)

where \( \mu^{(\alpha)} \) and \( \psi \) are the weighting functions for the Lagrange multiplier and deformation trace fields, respectively. Recalling that the total traction field is obtained by the summation of the partial tractions \( \lambda^{(\alpha)} \), we observe that (111) indeed imposes that the total traction equals the prescribed value \( \bar{T} \). For the case of a traction free surface, (111) also implies that the partial tractions are equal and opposite. Their value represents the magnitude of the force required to
hold the surfaces of the two constituents together to prevent relative separation. This surface force acts in tandem with
the interactive force to resist excessive relative motion of the solid constituents.

Remark. One physiological interpretation of the surface forces induced by the Lagrange multipliers is that they
correspond to the embedment zone or boundary layer of the domain where the scaffold fibers terminate and transfer
load into the matrix. In the homogenization process of mixture theory, the dimensions of this boundary layer are
not explicitly modeled. Consider for instance a constrained mixture consisting of orthogonal fibers and surrounding
matrix. Under uniaxial tension, the transverse fibers experience uniform “stress” throughout the domain, even at
the traction-free surfaces. The partial compressive stress in these fibers is balanced by a partial tensile stress in the
matrix, yielding zero effective mixture stress. These partial stresses develop in constrained mixture theory precisely
because the constituents deform together at all points. Recall also that the expressions for the interactive forces
given in Section 4.1 are functions of the constituent relative motion and vanish identically when the constituents
deform in tandem. Thus, effectively the Lagrange multipliers enforce that the mixture domain deforms in a manner
approximating constrained mixtures, and the interactive forces penalize the deviation of the constituent motion from
the constrained mixture solution. This observation is explored numerically through the test cases of Section 6.1.

This expanded system of equations can be solved in a staggered fashion, as advocated in [44], by alternating
between each constituent and the deformation trace field $\phi$. However, in our implementation we adopted a monolithic
solution strategy for (108)–(111) using a single Newton–Raphson loop due to the straightforwardness of the resulting
algorithm.

In order to further simplify the implementation of the coupled system (108)–(111), consider the auxiliary traction
variable $\tilde{\lambda}^{(s)} = \lambda^{(s)} + \tilde{T}$. Substituting $\tilde{\lambda}^{(s)}$ into (108)–(111) yields a modified system:

\begin{align}
\int_{V^{(s)}} \text{GRAD } w_{\phi}^{(s)} : p_{\phi}^{(s)} \, n_{V+1} \, dV - \int_{V^{(s)}} w_{\phi}^{(s)} \cdot J^{(s)}_{n+1} \, dV + \int_{\Gamma_{\phi}} w_{\phi}^{(s)} \cdot \tilde{\lambda}^{(s)} \, d\Gamma &= \int_{V^{(s)}} w_{\phi}^{(s)} \cdot \rho_{n+1}^{(s)} \, dV + \int_{\Gamma_{\phi}} w_{\phi}^{(s)} \cdot \tilde{T} \, d\Gamma \\
\int_{V^{(m)}} \text{GRAD } w_{\phi}^{(m)} : p_{\phi}^{(m)} \, n_{V+1} \, dV - \int_{V^{(m)}} w_{\phi}^{(m)} \cdot J^{(m)}_{n+1} \, dV + \int_{\Gamma_{\phi}} w_{\phi}^{(m)} \cdot \lambda^{(m)} \, d\Gamma &= \int_{V^{(m)}} w_{\phi}^{(m)} \cdot \rho_{n+1}^{(m)} \, dV \\
\int_{\Gamma_{\phi}} \mu^{(s)} \cdot (\tilde{\phi}^{(s)} - \phi) \, d\Gamma &= 0, \quad \int_{\Gamma_{\phi}} \mu^{(m)} \cdot (\tilde{\phi}^{(m)} - \phi) \, d\Gamma &= 0 \\
\int_{\Gamma_{\phi}} \psi \cdot (\tilde{\lambda}^{(s)} + \lambda^{(m)}) \, d\Gamma &= 0.
\end{align}

We observe that the surface equilibrium equation (115) is identical to (111) with $\tilde{\lambda}^{(s)}$ taking the place of $\lambda^{(s)}$,
and the external mixture traction $\tilde{T}$ can be viewed as a traction field “applied” to the scaffold constituent. Namely,
the computed solution to (112)–(115) is identical to (108)–(111) except for the single field $\tilde{\lambda}^{(s)}$; in particular, the
deformation and stress fields of the constituents remain unaltered. This modified formulation naturally accommodates
implementations for homogeneous boundary constraint equations and utilizes existing modules for applying surface
tractions within solid mechanics finite element codes. Note that a similar redefinition could be applied to the matrix
$\lambda^{(m)}$; thus, the choice of the constituent to “apply” the mixture traction onto is arbitrary.

6. Simulation and results

We investigate the attributes of the proposed mixture theory from Sections 3 and 4 and associated finite element
formulation from Section 5 through a series of numerical studies. First, the two growth models are evaluated in the
case of spatially uniform material parameters and internal stress. Then, the density growth model is investigated for
non-uniform growth rates. All calculations are performed using trilinear hexahedral pure-displacement elements with
full integration via eight point Gauss quadrature.
Each numerical study is performed on a 10 cm \( \times \) 10 cm rectangular specimen lying in the \( x - y \) plane with a 1 cm thickness in the \( z \) direction, as seen in Fig. 5. Symmetry conditions (smooth rollers) are applied on each of the faces \( x = 0, y = 0, \) and \( z = 0 \). The prescribed external loading is applied at the \( x = 10 \) specimen face, either prescribed traction for the density growth model or prescribed displacement for the volume growth model. The fibers forming the unidirectional scaffold are taken to be aligned with the \( y \)-axis (\( \mathbf{m} = e_y \)), indicating the direction of the anisotropy of the scaffold as well as the axis of cylindrical growth of the volumetric model. The moduli for each constituent are listed in the following sections. Additionally, the constituents are tied together along the exposed faces \( y = 10 \) and \( z = 1 \) using the Lagrange multiplier technique proposed in Section 5.2, thus leading to traction-free surfaces on the mixture.

While this rectangular domain may appear simplistic, it is nonetheless representative of a mechanical state experienced by a neighborhood of material points within a larger tissue or organ. Additionally, the mixture theory representation of this neighborhood retains the effects of each separate constituent which experience interactions from one another through the interactive force and mass exchange terms. This is in contrast to typical homogenization methods which arrive at a single effective material and no longer provide the distinctive mechanical response of each constituent.

6.1. Consistent partial tractions via Lagrange multipliers

The first numerical problem demonstrates the utility of the surface Lagrange multiplier formulation described in Section 5.2 for determining the consistent partial tractions for Neumann boundary conditions. The rectangular domain in Fig. 5 is subjected to uniaxial tension first through prescribed displacements and then through prescribed tractions. For simplicity, the isotropic material model given by (73) is applied for both mixture constituents in order to provide an exact solution. The “soft” material is assigned \( E_{\text{M,soft}} = 1 \) MPa while a larger modulus \( E_{\text{M, stiff}} = 4 \) MPa is assigned to the “stiff” material; both constituents have \( \nu_{\text{M}} = 0.3 \) so that their transverse contraction is the same when a common longitudinal strain is applied. The true density is \( \rho(s) = 1200 \text{ kg/m}^3 \times h^2/s^2 \) and the coefficient for the cohesive interactive force is \( k_U = 2 \times 10^9 \text{ N/m}^4 \). A structured mesh containing \( 2 \times 2 \times 2 \) elements is used for the finite element simulation, and the prescribed boundary conditions are applied to the face \( x = 10 \) cm. Growth is precluded in both constituents; therefore, the problem is solved in one load step in a quasi-static manner.

The first loading case consists of a prescribed displacement \( u_x = 2.0 \) mm which axially extends the mixture domain. Lagrange multipliers are applied on the surfaces \( y = 10 \) and \( z = 1 \) to tie the constituents together. The resulting partial Cauchy stresses \( \sigma_{xx} \) in the soft and stiff constituents is shown in Fig. 6. The exact numerical values are respectively 19.934 kPa and 79.736 kPa. The sum of these partial stresses yields a mixture Cauchy stress \( \sigma_{xx} = 99.670 \) kPa, which matches exactly with the result expected from constrained mixture theory for two constituents loaded in parallel with \( E_{\text{M, mixture}} = E_{\text{M, soft}} + E_{\text{M, stiff}} = 5 \) MPa. Each constituent experiences equal axial and transverse strains, and the other stress components vanish identically. The computed displacements for the point \((x, y, z) = (10, 10, 1)\) cm are \((-2, -0.59372, -0.05937)\) mm.

Next, the mixture domain is subjected to a prescribed traction on the \( x = 10 \) face. Lagrange multipliers are applied to all 3 exposed faces of the domain, including the face where the traction is applied. The magnitude of the traction is
set to 98.490 kPa in the material configuration, corresponding to the first Piola–Kirchoff stress of the mixture under the first loading case. This traction is applied completely to the “soft” constituent within the finite element model. However, the resulting solution is identical to the one shown in Fig. 6, and the computed displacement of the mixture domain is again \((2, -0.59372, -0.05937)\) in the corner \((x, y, z) = (10, 10, 1)\). Therefore, the Lagrange multipliers lead to the correct partitioning of the traction applied to the soft and stiff constituents through the weak enforcement of common deformations on each of the exposed domain surfaces.

As a third example, the prescribed traction problem is solved again, but without the Lagrange multiplier fields on the exposed surfaces. Here, the computed stress fields in the constituents are no longer uniform, as illustrated in Fig. 7. Recall that the 98.490 kPa surface traction is applied to the soft constituent. Thus, this constituent experiences larger partial stresses near the surface \(x = 10\) compared to Fig. 6(a). Also, the stiff constituent “sees” a traction-free edge at \(x = 10\). The levels of stress approach the values observed in Fig. 6(a) and (b) near to the other face \(x = 0\) of the domain.

The discrepancy in partial stresses is accompanied by large relative deformation of the constituents, shown for the soft and stiff constituents in Fig. 8(a) and (b), respectively. The deformation of the soft constituent is larger and exceeds the “exact” 2.0 mm displacement since the full traction is applied to this constituent. The stiff constituent maximum deformation is about 1.5 mm at the face \(x = 10\). Clearly, a significant portion of the soft constituent has protruded from the stiff constituent at this location; their relative deformation is lower as the face \(x = 0\) is approached. Also, the variation of displacement is piecewise linear within each constituent rather than having a constant spatial gradient, as exhibited by the difference in the color variation of the contours in Fig. 8(a) and (b).

The constituent relative deformation gives rise to a non-zero interactive force, which is shown in Fig. 9. The magnitude of the force is reasonable taking account of (70), the relative deformation of the elements \(\phi^{(2)} - \phi^{(1)} = 0.0015\) m near the right side of the domain in Fig. 8, and the cohesion coefficient \(k_U = 2 \times 10^9\) N/m\(^4\). This force is generated by the soft constituent dragging through the stiff one, gradually transferring the applied stress along the path from \(x = 10\) to \(x = 0\) (see Fig. 7). The features of this computed solution indicate that the interactive force does not completely preclude the protrusion of one constituent from the other. In fact, inspection of (70) reveals that \(f_{coh}^{(a)}\) is nonzero if and only if the constituents experience relative motion and is zero if and only if no relative motion occurs.
Fig. 8. Displacement contours \( u_x \) (mm) on deformed configuration: (a) soft constituent; (b) stiff constituent. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 9. Cohesive-based interactive force \( F_i^{(1)} \) (N/m³).

Rather, the surface Lagrange multipliers are required in order that prescribed traction is consistently applied in the correct fraction to each constituent leading to the expected homogeneous deformation presented in Fig. 6.

**Remark.** This simple numerical test substantiates the observations of Section 5.2 that the Lagrange multiplier fields enforce the features of constrained mixture response along the domain boundary while the interactive force impacts the relative motion within the mixture interior. Thus, the homogeneous mechanical deformations for the studies in Sections 6.2 and 6.3 do not generate interactive forces. Rather, these forces emerge alongside the inhomogeneous stress state exhibited by the differential growth problem presented in Section 6.4.

### 6.2. Parametric study of density growth model

The density growth model is considered first with uniform material parameters specified throughout the domain, as listed in Table 3. The matrix properties \( E_M \) and \( \nu_M \) contribute to the constitutive model for the matrix constituent from Section 4.3 as well as the homogenized scaffold constituent from Section 4.2. The modulus of the fibers is taken as \( E_S \), which is larger than the matrix modulus. Also, the volume fraction \( \pi_0(\alpha) \) is assumed for each constituent, and the homogenization factor in (72) is set to \( \beta = 1 \). Lastly, while the drag coefficient for the interactive force is specified, the interactive force vanishes for this problem due to the spatially uniform stress field; see the balance of linear momentum (36).

A structured mesh containing \( 2 \times 2 \times 2 \) elements is used for the finite element simulation, as shown in Fig. 10. The prescribed external surface traction of 50 kPa is applied to the face \( x = 10 \) instantaneously at time \( t = 0 \) h and held constant during the simulation. This applied force induces growth in the matrix of cells over time until a homeostatic equilibrium is achieved. The numerical simulation is performed with time step size of \( \Delta t = 100 \) h up to a final time of 5000 h.

Contour plots of the partial stress fields \( \sigma_{xx} \) for the scaffold and matrix constituents are provided in Fig. 10 at the model times \( t = 100 \) h and \( t = 2000 \) h. The computed stress fields are spatially uniform, which is consistent with
Table 3
Material and density growth parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_M$</td>
<td>50 MPa</td>
</tr>
<tr>
<td>$\nu_M$</td>
<td>0.2</td>
</tr>
<tr>
<td>$E_S$</td>
<td>125 MPa</td>
</tr>
<tr>
<td>$\pi_0^{(s)}$</td>
<td>0.5</td>
</tr>
<tr>
<td>$\pi_0^{(m)}$</td>
<td>0.5</td>
</tr>
<tr>
<td>$A$</td>
<td>$2 \times 10^9$ N h/m$^4$</td>
</tr>
<tr>
<td>$\rho_0^{(s)}$</td>
<td>2.0</td>
</tr>
<tr>
<td>$\rho_0^{(m)}$</td>
<td>1.0</td>
</tr>
<tr>
<td>$\rho_R$</td>
<td>$1200$ kg/m$^3 \times h^2/s^2$</td>
</tr>
<tr>
<td>$\rho_R^{(m)}$</td>
<td>$1200$ kg/m$^3 \times h^2/s^2$</td>
</tr>
</tbody>
</table>

Fig. 10. Stress $\sigma_{xx}$ (kPa) contours for density growth: (a) scaffold, $t = 100$ h; (b) matrix, $t = 100$ h; (c) scaffold, $t = 2000$ h; (d) matrix, $t = 2000$ h.

the applied boundary conditions and material parameters. Notice that the stress in the matrix increases over time; this indicates that the matrix stiffness has increased due to the stress-driven density growth process. The stiffening of the matrix leads to an unloading of the scaffold constituent, since the applied stress is maintained at 50 kPa.

The computed displacement field $(u_x, u_y, u_z)$ at the point $(10, 10, 1)$, partial stresses, and matrix grown density are recorded in Table 4 for the conclusion of the simulation. The magnitude of the deformations is small, which is appropriate for hard tissue mechanics such as bone growth. Notice that the sum of the partial stresses $\sigma_{xx}$ times the deformed surface area is equal to the applied (dead) force of 50 Newton. Also, the transverse partial stresses are equal and opposite. Recall that the scaffold is stiffened in the $y$-direction due to the fibers. However, the two constituents are enforced to deform equally along the transverse face due to the Lagrange multiplier constraint. Thus, since the matrix is less stiff than the scaffold, the compatible deformed shape results in compression in the scaffold and tension in the matrix. The density of the matrix is also observed to increase rather significantly, corresponding to a multiple of 5.64 times the initial density $\rho_0^{(m)} = 600$.

Next, the parameter $m_\rho$ in the matrix constitutive model (78) is studied to determine its effect on the overall mixture response. The representative values $[1.50, 2.00, 2.50, 3.00]$ are chosen, and simulations are performed keeping the geometry, loading, and other parameters fixed. The response of the corner displacement, partial stresses, and matrix density during the 5000 h growth period are plotted in Fig. 11. Similar to the study of the mass exchange term performed for open system mechanics [23], larger values of $m_\rho$ are found to decrease the growth rate of the density.
Table 4
Solution fields for density growth at $t = 5000$ h.

<table>
<thead>
<tr>
<th>Field</th>
<th>Value</th>
<th>Field (kPa)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$u_x$ ($\mu$m)</td>
<td>29.231</td>
<td>$\sigma_{xx}^{(m)}$</td>
<td>7.533</td>
</tr>
<tr>
<td>$u_y$ ($\mu$m)</td>
<td>1.5017</td>
<td>$\sigma_{yy}^{(m)}$</td>
<td>42.471</td>
</tr>
<tr>
<td>$u_z$ ($\mu$m)</td>
<td>-0.69313</td>
<td>$\sigma_{zz}^{(m)}$</td>
<td>-6.376</td>
</tr>
<tr>
<td>$\rho_{\phi}^{(m)}$ (kg/m$^3$ x h$^2$/s$^2$)</td>
<td>3,382.2</td>
<td>$\sigma_{yy}^{(m)}$</td>
<td>6.376</td>
</tr>
</tbody>
</table>

Fig. 11. Evolution of constituent solution fields for values of $m_{\rho}$ (scaffold denoted with solid lines, matrix denoted with symbols): (a) density $\rho_{\phi}^{(m)}$; (b) displacement $u_z$ of free edge; (c) Cauchy stress $\sigma_{xx}$; (d) Cauchy stress $\sigma_{yy}$. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Higher density of the matrix constituent also induces higher apparent stiffness of the mixture, which reduces the magnitude of deformation over time as seen in Fig. 11(b). The $z$-component of displacement exhibited the largest variation as a function of the density growth exponent $m_{\rho}$. For the partial stress fields, both of the constituents are plotted on the same axes in Fig. 11(c) and (d), with the scaffold denoted by curves and the matrix denoted by symbols. The axial stress field has larger sensitivity compared to the transverse stress field. The evolution of stress over time agrees with the contour plots shown in Fig. 10.

An additional parametric study was performed for $\psi_{\phi}^{(m)}$, and the time-history results of the solution are given in Fig. 12. We conclude that this parameter controls the saturation amount of growth, as indicated by the difference in asymptotic values for density obtained in Fig. 12(a). Similar trends in the displacement field and partial stresses are apparent as compared to the preceding study for $m_{\rho}$. However, for the range of parameters chosen, the equilibrium density shows a much wider variation.
Fig. 12. Evolution of constituent solution fields for values of $\psi_s^{(m)}$ (scaffold denoted with solid lines, matrix denoted with symbols): (a) density $\rho_s^{(m)}$; (b) displacement $u_z$ of free edge; (c) Cauchy stress $\sigma_{xx}$; (d) Cauchy stress $\sigma_{yy}$.

Table 5
Material and volumetric growth parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_M$</td>
<td>1 MPa</td>
</tr>
<tr>
<td>$\nu_M$</td>
<td>0.3</td>
</tr>
<tr>
<td>$E_S$</td>
<td>4 MPa</td>
</tr>
<tr>
<td>$\pi_0^{(s)}$</td>
<td>0.5</td>
</tr>
<tr>
<td>$\pi_0^{(m)}$</td>
<td>0.5</td>
</tr>
<tr>
<td>$A$</td>
<td>$2 \times 10^9$ N h/m$^4$</td>
</tr>
<tr>
<td>$k_T^{(s)}$</td>
<td>0.5 (MPa h)$^{-1}$</td>
</tr>
<tr>
<td>$k_T^{(m)}$</td>
<td>0.5 (MPa h)$^{-1}$</td>
</tr>
<tr>
<td>$\rho_R^{(s)}$</td>
<td>1000 kg/m$^3 \times$ h$^2$/s$^2$</td>
</tr>
<tr>
<td>$\rho_R^{(m)}$</td>
<td>1000 kg/m$^3 \times$ h$^2$/s$^2$</td>
</tr>
</tbody>
</table>

We wish to highlight the difference in the computed response between the $\sigma_{xx}$ and $\sigma_{yy}$ partial stresses. While the matrix constituent stress $\sigma_{xx}$ varies between 30 and 42 MPa as a function of density, the transverse stress $\sigma_{yy}$ varies only slightly between 6 and 7 MPa. This dependence on the material parameters as well as the evolution of stress over time substantiates our claim that the mixture framework provides a means to capture the evolving anisotropy of the specimen.

6.3. Parametric study of volumetric growth model

The second study is performed on the same rectangular domain, but the constituent constitutive models now correspond to the volumetric growth model from Section 4.4. The material parameters listed in Table 5 are adapted from a model for volumetric growth developed in open system mechanics [32]; again, the scaffold fibers are considered as stiffer than the matrix.

Similar to the example in Section 6.2, a structured $2 \times 2 \times 2$ element mesh is employed, and the simulation proceeds at time steps of $\Delta t = 100$ h up to a final time of 5000 h. However, the applied loading is now an instantaneous axial elongation of the domain, with a prescribed displacement $u_x = 2$ mm on the face $x = 10$ at time $t = 0$. This
Table 6
Solution fields for volumetric growth at \( t = 5000 \) h.

<table>
<thead>
<tr>
<th>Field</th>
<th>Value</th>
<th>Field (kPa)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( u_x ) (mm)</td>
<td>( 2.0000 \times 10^0 )</td>
<td>( \sigma^{(s)}_{xx} )</td>
<td>7.2717</td>
</tr>
<tr>
<td>( u_y ) (mm)</td>
<td>( -3.3528 \times 10^{-2} )</td>
<td>( \sigma^{(m)}_{xx} )</td>
<td>11.7798</td>
</tr>
<tr>
<td>( u_z ) (mm)</td>
<td>( -4.9552 \times 10^{-2} )</td>
<td>( \sigma^{(s)}_{yy} )</td>
<td>1.2875</td>
</tr>
<tr>
<td>( \nu - 1 ) (stretch)</td>
<td>( 4.7734 \times 10^{-3} )</td>
<td>( \sigma^{(m)}_{yy} )</td>
<td>-1.2875</td>
</tr>
</tbody>
</table>

The computed solution to this problem also possesses spatially uniform stress fields similar to the density growth problem. Therefore, we do not report the contour plots here. Instead, the values of the solution field at the end of the simulation at time \( t = 5000 \) h are provided in Table 6. Recall that the cylindrical growth takes place in the \( x - z \) plane, orthogonal to the fiber orientation vector \( m \). The growth stretch ratio has approached the saturation value of \( \nu^+ = 1.005 \). Also, the transverse stresses \( \sigma_{yy} \) in the constituents have reversed compared to the density growth simulation. To explain this result, note that the matrix does not expand or contract much in the \( y \) direction because of the alignment of the cylindrical growth. However, the scaffold contracts in the \( y \) direction when it is pulled in the \( x \) direction. Thus, the scaffold compresses the matrix inward while the matrix extends the scaffold in the \( y \) direction, leading to the tension and compression shown in Table 6.

Parametric studies are now conducted to determine the effects of \( k^+ \) and \( m_\nu \) in the growth constitutive model. The results for the \( k^+ \) study are shown in Fig. 13, where we observe that increasing this parameter leads to a decrease in the amount of time elapsed until the saturation stretch ratio is met. Similar to the density growth model, for this choice of material parameters, the matrix constituent carries a larger axial stress compared to the scaffold constituent as seen in Fig. 13(b). Also, the matrix stress was not sensitive to the material parameter \( k^+ \), but the rate of relaxation of the scaffold stress showed a greater correlation. More significant trends are visible in the transverse stress components \( \sigma_{yy} \) and \( \sigma_{zz} \) in Fig. 13(c) and (d), respectively. The constituents each experience equal and opposite stresses, and the rate of relaxation directly correlates to the growth rate. Notice that the stresses in the two directions show opposite behavior for which constituent experiences tension or compression.

Reverse trends are observed for the parameter study of \( m_\nu \) in Fig. 14; for larger values, the elapsed time to reach the growth saturation increases. At the value \( m_\nu = 1.25 \), the volumetric growth is almost instantaneous. For parameter values between 2.0 and 4.0, the evolution over time of the stretch ratio in Fig. 14(a) is fairly similar. However, the partial stresses in the constituents exhibit greater variability to the material parameter, especially the \( \sigma_{zz} \) field in Fig. 14(d).

6.4. Differential growth rate for density growth model

For the last numerical study, the density growth specimen is revisited with one significant change: the growth exponent \( m_\rho \) is prescribed with a non-uniform value throughout the domain. The parameter is varied from \( m_\rho = 1.5 \) at \( x = 10 \) to \( m_\rho = 3.0 \) at \( x = 0 \), with a constant value in each element, as shown in Fig. 15. A finer mesh of 256 elements is used in order to resolve the variation in the fields throughout the domain. According to Fig. 11(a), these parameter values imply that growth is faster on the right side of the domain and slower on the left. Physically, this variation could be attributed to a concentration gradient of the nutrient constituent, perhaps due to a concentrated source at \( x = 10 \) that diffuses toward the left end of the mixture. We remark that this problem could be extended by expressing these material parameters directly as a function of the nutrient concentration and then treating this concentration as an additional solution field.

6.4.1. Effect of spatial variation of the density growth rate on matrix density evolution

All other material parameters are maintained from Table 3, and a tensile traction of 50 kPa is applied instantaneously along the \( x = 10 \) face. However, the spatial variation of \( m_\rho \) is expected to have significant impact.
Fig. 13. Evolution of constituent solution fields for values of $k^+_v$ (scaffold denoted with solid lines, matrix denoted with symbols): (a) stretch ratio $\nu$; (b) Cauchy stress $\sigma_{xx}$; (c) Cauchy stress $\sigma_{yy}$; (d) Cauchy stress $\sigma_{zz}$.

on the response of the mixture. In particular, the inhomogeneous response provides a test case for comparing the interactive force models proposed in Section 4.1.

The evolution of the density field $\rho^{(m)}$ within the specimen is presented in Fig. 16 as a series of snapshots. Note that the density field, as well as the stress contours presented in later figures, has been projected from the integration points and averaged at the nodes of the mesh in order to plot a smooth contour. Since a rather uniform value of stress is expected throughout the specimen, the rate of growth at various locations should mostly be controlled by the value of $m_\rho$ and correspond with the results from Section 6.2. This hypothesis is confirmed in Fig. 16. Observe that the density at $x = 10$ is about 4000, which is similar to the density value from the spatially uniform growth simulation in Fig. 11(a) for the blue-solid curve $m_\rho = 1.5$. Meanwhile, the opposite end of the domain has densified less, reaching only 2500, which again qualitatively matches with the black-dashed curve in Fig. 11(a) for $m_\rho = 3.0$. Also, the variation of the density in the $y$ and $z$ directions is negligible.

To investigate the response of the mixture constituents, the partial stresses $\sigma_{xx}$ in the scaffold and matrix are presented in Fig. 17 on the material configuration at the time levels $t = 1000$ h and $t = 4000$ h. Similar to the results in Section 6.2, the portion of the applied traction carried by the matrix increases over time while the scaffold portion decreases. However, the differential growth rate leads to a differential rate for this stress redistribution as well. As expected, the region of faster growth at $x = 10$ exhibits higher stresses compared to the $x = 0$ region. This stress differential is about 3 kPa, which is about 10%–20% of the applied traction. Also, slight variations in the stress fields from the $y = 0$ face to the $y = 10$ can be observed.

To further quantify the spatial variation of the specimen response, the shear stress field $\sigma_{xz}$ is presented in Fig. 18. While these stresses vanished during the uniform growth cases, the combination of the variable growth rate, stress differential, and traction and displacement boundary conditions leads to a non-uniform value of the shear stress. Comparing both Fig. 18 (a) and (c) along with (b) and (d), the partial stresses are found to be equal and opposite between the constituents. Also, the stress on the exposed surface $z = 1$ appears to increase over time. These increased
Fig. 14. Evolution of constituent solution fields for values of $m_\nu^+$ (scaffold denoted with solid lines, matrix denoted with symbols): (a) stretch ratio $\nu$; (b) Cauchy stress $\sigma_{xx}$; (c) Cauchy stress $\sigma_{yy}$; (d) Cauchy stress $\sigma_{zz}$.

Fig. 15. Spatial variation of growth parameter $m_\rho$.

Shear stresses could be attributed to the surface tying of the mixture constituents along the traction-free surfaces. As mentioned in Section 5.2, the entire displacement vector from each constituent is enforced to match at each point along the surface, rather than a relaxed constraint of only matching the normal component of the displacement field. The actual conditions of the bonding of the constituents play a major role as to whether this mathematical assumption is an accurate representation of the physical system.

6.4.2. Comparison of interactive force constitutive models

Next, we investigate the interactive forces generated during this non-uniform growth simulation. These results are unique to the present mixture formulation, since interactive forces do not appear within the constrained mixture
Fig. 16. Matrix density \( \rho^{(m)} \) (kg/m\(^3\) \( \times \) h\(^2\)/s\(^2\)): (a) time \( t = 100 \) h; (b) time \( t = 1000 \) h; (c) time \( t = 2000 \) h; (d) time \( t = 5000 \) h.

Fig. 17. Stress contours \( \sigma_{xx} \) (kPa) within mixture domain: (a) matrix, \( t = 1000 \) h; (b) matrix, \( t = 4000 \) h; (c) scaffold, \( t = 1000 \) h; (d) scaffold, \( t = 4000 \) h.
formulations for solid constituent mixtures. This model problem was conducted using all three constitutive expressions for the interactive force from Section 4.1. The preceding contour plots for density and stress correspond to the incompatibility-based force (69), with a value $k = 1$ for the proportionality coefficient. The choice of the interactive force did not significantly affect the density field or the $\sigma_{xx}$ field.

The evolution of the interactive force component acting from the matrix onto the scaffold is shown in Figs. 19 and 20, in units of Newton/m$^3$. Notice that the drag-based forces are initially large just after the load is applied, which indicates that relative velocity exists between the scaffold and matrix. Thus, while the boundaries of the mixture are enforced to conform, the inter-constituent motion on the interior of the domain is counteracted by the interactive force. The drag-based force decays over time to a small magnitude at $t = 5000$ h. This result makes sense because the model is velocity-based. Once the solid constituents stop deforming relative to each other, this force will decay. Crucially, the force does not depend on whether the constituents have displaced with respect to each other, only whether the time derivative of this displacement is not equal. While this constitutive model is attractive for modeling fluid–fluid or solid–fluid interactions, this behavior may not be appropriate for solid–solid interaction.

In contrast, the incompatibility-based interactive forces remain non-zero during the entire simulation. Also, they have a relatively large value for both the $x$ and $z$ components, while only the $x$ component of the drag-based force is substantial. The $z$ component of $I^{(\psi)}$ exhibits larger values near the edges of the rectangular domain. These concentrations may be attributed to the transition from traction-free to displacement-prescribed boundary conditions, or also due to the full constraint enforced by the Lagrange multiplier field. Further studies on the interactive force are necessary in order to quantify its contribution and to further evaluate possible constitutive expressions.

These results are compared with those corresponding to the cohesion-based interactive force presented in Fig. 21. The cohesion coefficient is set to $k_U = 2 \times 10^7$ N/m$^4$, which is smaller than the value applied in Section 6.1 such that the expected value of $I^{(m)}_{\text{coh}}$ matches with that of $I^{(m)}_{\text{drag}}$ due to the velocities experienced during the time step $\Delta t = 100$ h. Indeed, the interactive forces observed at $t = 100$ h in Fig. 21(a) and (c) match closely to those for Fig. 19(b) and Fig. 20(b), respectively. In contrast to the drag-based interactive force, the results at $t = 5000$ h show a persisting force over time. The magnitude actually increases by about 30%–50% in portions of the domain, which
is consistent with the expected increases in incompatibility generated by the differential growth rates throughout the domain.

6.4.3. Mixture response assuming zero bound fraction between the matrix and scaffold

The preceding studies were performed using a homogenized scaffold constituent containing a portion of the stiffness associated with the matrix, which is assumed to be tightly bound to the scaffold fibers and does not experience growth. This fraction is specified through the factor $\beta$ in the constitutive model (72) of Section 4.2. To investigate the effect of removing the inherent transverse stiffness of the scaffold, the spatially variable growth simulation is performed again using $\beta = 0$. Also, the porosity of the matrix is modified to $\pi_0^{(m)} = 1.0$ to ensure that the same total fraction of the matrix is present; all other material parameters are retained (the value $\pi_0^{(s)} = 0.5$ is retained so that the scaffold fraction is also consistent). The cohesion-based interactive force is adopted for this example.

Fig. 22 presents the evolution of the matrix constituent density during the 5000 h model duration. The spatial distribution of density is similar to the bound matrix simulation results in Fig. 16. The observed density is slightly higher during the first time step (Fig. 22(a)), but the growth rate slows for the later time steps to yield values somewhat
Fig. 20. Interactive force $F_{\phi}^{(s)}$ (N/m$^3$) from each model: (a) incompatibility-based, $t = 100$ h; (b) drag-based, $t = 100$ h; (c) incompatibility-based, $t = 1000$ h; (d) drag-based, $t = 1000$ h; (e) incompatibility-based, $t = 5000$ h; (f) drag-based, $t = 5000$ h.

lower than those of Fig. 16. The total difference is about 10% by the last step $t = 5000$ h; thus, the modified treatment of the scaffold constitutive model induces a noticeable effect on the computed matrix response.

The contours of the partial Cauchy stress fields in the matrix and scaffold are reported in Fig. 23 for the model times 100 and 4000 h. The matrix $\sigma_{xx}$ stress remains approximately constant around 50 kPa during the simulation. This value is consistent with the total mixture longitudinal stress obtained in Section 6.4.1 determined by summing the matrix and scaffold stress contours in Fig. 17. Since the scaffold fibers are oriented in the $y$ direction, all stress components other than $\sigma_{yy}$ are zero for the scaffold constituent. Thus the matrix carries the total longitudinal stress. The transverse stress sustained by the fibers is compressive and decreases from Fig. 23(c) to (d). Thus, the stress in the fibers decreases in magnitude as the density of the matrix increases, whether from the spatial or temporal distribution.

Because of the removal of the scaffold transverse stiffness, the relative deformation of the two constituents under load is also expected to be different, which in turn affects the cohesion-based interactive force. Contour plots of the components of $F_{\phi}^{(s)}$ at two instances in time are shown in Fig. 24. These force distributions exhibit quite different characteristics from those obtained for the bound matrix simulations in Section 6.4.2. These component fields have nearly equal regions of positive and negative values, in contrast to Fig. 21 where negatively skewed values are observed for $F_{\phi}^{(s)}$. Also, the magnitude of the force decreases over time while the matrix density increases. These results
Fig. 21. Cohesive-based interactive force (N/m³): (a) $I_s^\phi(t), t = 100$ h; (b) $I_s^\phi(t), t = 5000$ h; (c) $I_z^\phi(t), t = 100$ h; (d) $I_z^\phi(t), t = 5000$ h.

Fig. 22. Matrix density $\rho_s^{(m)}$ (kg/m³ × h²/s²): (a) time $t = 100$ h; (b) time $t = 1000$ h; (c) time $t = 2000$ h; (d) time $t = 5000$ h.

confirm that the computed mixture response is sensitive to the choice of the constitutive functions for modeling the anisotropy and growth evolution of each constituent.
Fig. 23. Stress contours (kPa) within mixture domain: (a) matrix $\sigma_{xx}, t = 1000$ h; (b) matrix $\sigma_{xx}, t = 4000$ h; (c) scaffold $\sigma_{yy}, t = 1000$ h; (d) scaffold $\sigma_{yy}, t = 4000$ h.

Fig. 24. Cohesion-based interactive force (N/m$^3$) from each model: (a) $\sigma_{\phi}^{(s)}(x), t = 100$ h; (b) $\sigma_{\phi}^{(s)}(x), t = 5000$ h; (c) $\sigma_{\phi}^{(s)}(z), t = 100$ h; (d) $\sigma_{\phi}^{(s)}(z), t = 5000$ h.
7. Conclusion

We have developed a mixture theory and accompanying numerical formulation to model the interaction of multiple solid constituents in growing biological tissue. The thermodynamical framework for the mixture gives rise to the constitutive relations for two key features: the growth of solids by volume change or by densification, and the mechanical interactive forces between constituents. Herein, the theory is specialized to the case of two solid constituents (inert scaffold and growing matrix) and dispersed nutrient fluid. Each solid constituent is permitted to deform independently in contrast to the traditional constrained mixture hypothesis. The relative motion of constituents is counteracted by the interactive force, for which three constitutive models are proposed/investigated. Physically, the interactive force represents the incompatibilities that develop between the constituent microstructures in the deforming mixture (in a homogenized sense). The growth of the matrix constituent is treated as stress-driven, and the mechanical anisotropy of the mixture evolves with the change of relative density of the matrix and scaffold.

The finite element method for solving the mixture weak form consists of independent displacement interpolations for each constituent coupled by the interactive force terms. Accounting for the finite strain kinematics, the evaluation of the interactive force requires a closest-point projection algorithm to relate the constituents similar to contact mechanics formulations. Also, we propose a Lagrange multiplier treatment of the traction boundary conditions on the mixture surfaces, which previously was an unresolved issue for mixture theory. This formulation weakly enforces the overlapping constituent boundaries to deform together and consistently matches the applied traction to the partial stresses in each constituent.

Numerical tests on representative volumes within larger domains were conducted for both the density growth and volumetric growth constitutive models. Parametric studies revealed the influence of the applied stress on the growth rate and total density change. The degree of anisotropy exhibited by the mixture is found to evolve as the ratio of internal stresses in the scaffold and matrix constituents changes over time. Additionally, during the test of a specimen with spatially inhomogeneous properties, interactive forces were generated between the constituents. Results were compared for the simulations with the drag-type, incompatibility-based, and cohesive interactive forces. The proposed numerical formulation yielded stable and accuracy results for these benchmark problems.

Acknowledgments

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Appendix

Each of the constitutive models for the scaffold and matrix introduced in Section 4 is briefly reviewed, and additional constitutive tensors are provided to assist in their implementation into finite element codes.

The scaffold as described in Section 4.2 is represented by an anisotropic model with fiber orientation given by the unit vector \( \mathbf{m} \). The first Piola–Kirchhoff stress tensor is provided in Eqs. (74)–(75). The acoustic tensor of material moduli \( \mathbf{A} \) is obtained in component form by differentiating these expressions:

\[
\begin{align*}
\mathbf{A}^{(s)}_{ij, j} (\mathbf{F}) &= \pi_0 (s) \frac{\partial \mathbf{F}_{ij} (s)}{\partial \mathbf{F}_{jj}} = \pi_0 (s) \left[ \beta \mathbf{A}^{(M)}_{ij, j} (\mathbf{F}) + \mathbf{A}^{(S)}_{ij, j} (\mathbf{F}) \right] \\
\mathbf{A}^{(M)}_{ij, j} (\mathbf{F}) &= \mu_M \left( \delta_{ij} \delta_{1j} + \mathbf{F}_{ij}^{-1} \mathbf{F}_{ji}^{-1} \right) + \lambda_M \left( \mathbf{F}_{ij}^{-1} \mathbf{F}_{ji}^{-1} - \ln (J) \mathbf{F}_{ij}^{-1} \mathbf{F}_{ji}^{-1} \right) \\
\mathbf{A}^{(S)}_{ij, j} (\mathbf{F}) &= E_S \left( F_{kk} m_k F_{ll} m_l \delta_{ij} + 2 F_{ik} m_k F_{jl} m_l m_j \right)
\end{align*}
\]

where \( \delta_{ij} \) denotes the Kronecker delta, \( \mathbf{F} = F_{ij} \mathbf{e}_i \otimes \mathbf{e}_j \), \( \mathbf{F}^{-1} = F_{ji}^{-1} \mathbf{e}_i \otimes \mathbf{e}_j \), \( J = \det (\mathbf{F}) \), and summation is implied over repeated indices.

The density growth model for the matrix constituent is cited from [23] without modification. The implementation of this constitutive model using backward Euler discretization of the rate equation is described in [61]. We reproduce
the relevant equations below with the notation updated to the present mixture theory context.

\[
R_\rho = \left\{ \rho_\phi^{n+1} / \rho_0^{(m)} \right\}^{n_\rho-m_\rho} \rho_\phi^{n+1} \pi_0^{(m)} \psi_M - \psi_\psi^{(m)} \Delta t - \rho_\phi^{n+1} + \rho_\phi^n
\]  

(119)

\[
\partial_\rho_\rho R_\rho = (n_\rho - m_\rho) \left[ \rho_\phi^{n+1} / \rho_0^{(m)} \right]^{n_\rho-m_\rho} \pi_0^{(m)} \psi_M \Delta t - 1
\]  

(120)

\[
\Delta \rho_\rho = -R_\rho / \partial R_\rho
\]  

(121)

\[
\rho_0^{n+1} \leftarrow \rho_0^n + \Delta \rho_\rho
\]  

(122)

\[
\mathbf{A}_{ijj}^{(m)}(F) = \partial_F \mathbf{P}^{(m)} - \partial_\rho_\rho \mathbf{P}^{(m)} \left[ \partial_\rho_\rho R_\rho \right]^{-1} \partial_F R_\rho
\]  

(123)

\[
\left[ \partial_\rho_\rho \mathbf{P}^{(m)} \right]_{ijj} = \left[ \rho_\phi^{n+1} / \rho_0^{(m)} \right]^{n_\rho} \pi_0^{(m)} \mathbf{A}_{ijj}^{(M)}
\]  

(124)

\[
\left[ \partial_\rho_\rho \mathbf{P}^{(m)} \right]_{ijI} = (n_\rho / \rho_\phi^{n+1}) P_{II}^{(m)}
\]  

(125)

\[
\left[ \partial_\rho_\rho \mathbf{P}^{(m)} \right]_{jI} = \left( \rho_\phi^{n+1} / \rho_0^{(m)} \right)^{-m_\rho} P_{j}^{(m)}
\]  

(126)

where the expressions for certain quantities can be found in Sections 4.2 and 4.3: \( \psi_M \) is given by (73), \( \mathbf{P}^{(m)} \) is given by (75) and (80), and the other material parameters are defined in Section 4.3.

Finally, the volume growth model for the matrix constituent shares features with the isotropic growth model proposed in [32]. Again, a backward Euler scheme is applied to the stretch ratio evolution (84), which yields a nonlinear scalar equation that is iteratively solved using a Newton–Raphson approach. The relevant equations are expressed through the elastic deformation gradient \( \mathbf{F}_e^{(m)} \), and these are provided below as the result of the derivations.

\[
R_v = -v_{n+1} + v_\nu \left( v_{n+1} \right) \left[ M_{II}^{e} - m_1 M_{IJ}^{e} m_{J} \right]_{n+1} \Delta t
\]  

(127)

\[
\frac{\partial R_v}{\partial v_{n+1}} = 1 - \left[ \frac{\partial k_v}{\partial v_{n+1}} \left( M_{II}^{e} - m_1 M_{IJ}^{e} m_{J} \right) + k_v \left( \frac{\partial \left( M_{II}^{e} - m_1 M_{IJ}^{e} m_{J} \right)}{\partial v_{n+1}} \right) \right]
\]  

(128)

\[
\frac{\partial M_{LM}^{e}}{\partial F_{K}^{e}} m_{M} = m_1 \left[ P_{KLM}^{e} \partial F_{L}^{e} + A_{LMK}^{e} F_{L}^{e} \right] m_{M} = \left[ P_{KLM}^{e} m_{L} + A_{LMK}^{e} \left( F_{L}^{e} m_{L} \right) m_{M} \right]
\]  

(130)

\[
\frac{\partial F_{L}^{e}}{\partial v_{n+1}} = \frac{\partial \left( F_{L}^{e} M_{ML}^{e-1} \right)}{\partial F_{K}^{e}} = F_{L}^{e} \left[ -\frac{1}{u^2} \delta_{ML} + \frac{1}{u^2} m_{M} m_{L} \right]
\]  

(131)

\[
\frac{\partial \left( M_{II}^{e} - m_1 M_{IJ}^{e} m_{J} \right)}{\partial v_{n+1}} = k_v \left[ \frac{\partial M_{LM}^{e}}{\partial F_{K}^{e}} m_{M} - m_1 \frac{\partial M_{LM}^{e}}{\partial F_{K}^{e}} m_{M} \right] \frac{\partial F_{K}^{e}}{\partial v_{n+1}}
\]  

(132)

\[
\frac{\partial k_v}{\partial v_{n+1}} = \frac{m_{v}^{+}}{v_{n+1} - v_{\nu}^{+}} k_v \left( v_{n+1} \right) \text{ if } \left( M_{II}^{e} - m_1 M_{IJ}^{e} m_{J} \right) > 0
\]  

(133)

\[
\frac{\partial k_v}{\partial v_{n+1}} = \frac{m_{v}^{-}}{v_{n+1} - v_{\nu}^{-}} k_v \left( v_{n+1} \right) \text{ if } \left( M_{II}^{e} - m_1 M_{IJ}^{e} m_{J} \right) < 0
\]  

(133)

in which the classical acoustic material tensor \( A_{ijj}^{e} \equiv \partial P_{ij}^{e} / \partial F_{jj}^{e} \) from (117), and the expressions for \( P_{ij}^{e} \) and \( F_{ij}^{e} \) are given by (87) and (82), respectively. Iteration on the value of the stretch ratio \( v_{n+1} \) is carried out until a convergence criterion is satisfied:

\[
\text{for } i = 1, 2, \ldots \text{ } \Delta v_{n+1}^i = R_{v}^i / \partial_\nu \nu \nu^i \quad \nu_{n+1}^i = \nu_{n+1}^i + \Delta v_{n+1}^i.
\]  

(134)

Upon convergence, the stretch ratio \( v_{n+1} \) can be substituted into the kinematic formula (82) to subsequently enable the computation of \( P_{ij}^{e} \) according to (87).
Lastly, the algorithmic tangent required in the evaluation of the consistent tangent matrix is obtained by differentiating the algorithmic stress tensor:

\[
A^{eg}_{iLJ} = \frac{\partial P_{iL}}{\partial F_{fJ}} = \frac{\partial P^e_{kK}}{\partial F^e_{kK}} \left( \frac{\partial F^e_{Ij}}{\partial F_{fJ}} + \frac{\partial F^e_{kK}}{\partial u} \frac{\partial u}{\partial F_{fJ}} \right) F^{-1}_{IL} + P^e_{fL} \frac{\partial F^e_{fL}}{\partial F_{fJ}}.
\] (135)

The first term represents the classical acoustic tensor modified by a relation of the elastic to total deformation:

\[
\frac{\partial F^e_{kK}}{\partial F_{fJ}} = \frac{\partial \left( F^e_{kL} F^{-1}_{kL} \right)}{\partial F_{fJ}} = \delta_{kj} F^{-1}_{jK}
\] (136)

\[
\frac{\partial F^{-1}_{fL}}{\partial F_{fJ}} = \frac{\partial F^{-1}_{fL}}{\partial u} \frac{\partial u}{\partial F_{fJ}}.
\] (137)

The second term reflects the correction arising from the evolution of the growth stretch ratio. We summarize the lengthy derivation of the component terms in the following:

\[
\frac{\partial u}{\partial F_{fJ}} = (\bar{\partial}_u \bar{u})^{-1} (\Delta t) k_u \left[ \frac{\partial M^e_{fL}}{\partial F^e_{kK}} - m\frac{\partial M^e_{fL}}{\partial F^e_{kK}} m_M \right] \frac{\partial F^e_{fL}}{\partial F_{fJ}}.
\] (138)

References


