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A formulation of volumetric growth as a mechanical problem subjected to non-holonomic and rheonomic constraint

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Abstract

Starting from a reformulation of the mass balance law based on the Bilby-Kröner-Lee (BKL-) decomposition of the deformation gradient tensor, we study some peculiar mechanical aspects of growth in a monophasic continuum by regarding the reformulated mass balance equation as a non-holonomic and rheonomic constraint. Such constraint restricts the admissible rates of the growth tensor, i.e., one of the two factors of the BKL-decomposition, to comply with a growth law provided phenomenologically. For our purposes, we put the constraint in Pfaffian form, and treat time as a fictitious, additional Lagrangian parameter, subjected to the condition that its rate must be unitary. Then, by taking some suggestions from the literature, we assume the existence of generalized forces conjugated with the virtual variations of the growth tensor, and we write a constrained version of the Principle of Virtual Work (PVW) that leads to a mixed boundary value problem whose unknowns are the motion, the growth tensor, and the Lagrange multipliers of the considered theory. This allows to extrapolate a physical interpretation of the role that the growth-conjugated forces play on the components of the growth tensor, especially on the distortional ones, i.e., those that are not directly related to the variation of mass of the body. The core message of our work is conceptual: we show that the growth laws usually encountered in the literature, which are prescribed phenomenologically, but may be difficult to justify theoretically, can be put in the framework of the Principle of Virtual Work by regarding them as constraints. Moreover, we retrieve more particularized frameworks of growth available in the literature, while being able to switch to a theory of growth of grade one, such as a Cahn-Hilliard model of growth.

Keywords

Growth mechanics; Bilby-Kröner-Lee multiplicative decomposition; Non-holonomic constraints; Lagrange multipliers; Principle of Virtual Work; Dissipation; Cahn-Hilliard model.

1 Introduction

In Mechanics, the Principle of Virtual Work (PVW)¹ constitutes a well-established paradigmatic method for determining the conditions of (dynamic) equilibrium for systems with finite number of

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¹In this work, we refer to the Principle of Virtual Work (PVW) in a generalized sense, thereby including also D’Alembert’s Principle. In Continuum Mechanics, this can be done by counting inertial forces among the body forces

29 degrees of freedom (see e.g. [87, 14, 17, 47]). Even in the presence of holonomic constraints, be they
 30 rheonomic (i.e., explicitly time-dependent) or not, or of non-holonomic and scleronomic (i.e., not
 31 explicitly dependent on time) constraints, the *Lagrange multiplier method* makes the constrained
 32 version of the PVW a straightforward generalization of the case in which such constraints are absent
 33 [87]. However, to the best of our knowledge, the formulation of the PVW becomes less obvious
 34 when the considered constraints are non-holonomic *and* rheonomic, although constraints of this
 35 type are the focus of several studies [106, 92, 121, 95, 104, 91], especially after the formulation of
 36 the so-called *vakonomic dynamics* due to Kozlov [82, 83, 84, 85].

37 In Continuum Mechanics, the PVW has a rather long history, too (see e.g. [52]), and, as reported
 38 by Germain [53], it has been employed in an increasingly consistent manner for determining the
 39 balance of forces at the basis of the continuum theories developed through the years. By virtue
 40 of the intrinsic elegance of its formulation, which has its origin in the concept of duality between
 41 kinematics and dynamics, the PVW puts naturally Mechanics in the framework of Differential
 42 Geometry, as suggested by Epstein and Segev [42], Marsden and Hughes [98], and many other
 43 authors.

44 In addition to the problems involving “non-classical” continua, such as beams and plates [33]
 45 modeled after Cosserat media [29], materials with microstructure [53, 103, 119, 21], micromorphic
 46 and micropolar media [60, 43], or multipolar media [61], and generalized continua [34], the PVW
 47 has been used extensively also in the context of the mechanics of inelastic phenomena, such as
 48 standard and strain gradient plasticity [32, 75], where it served as a point of departure for re-
 49 interpreting the theories proposed, for example, by Aifantis [3, 4], or for developing new theories
 50 [71, 72, 73], and performing studies based on such theories [13, 69].

51 In some of the above referenced works (see e.g. [71, 73]), the theory is accompanied by con-
 52 straints imposed on the tensor field that describes the plastic distortions, which are indeed assumed
 53 to be isochoric, and associated with null plastic spin. In this respect, the elastoplasticity developed
 54 by Gurtin and Anand [71, 73] is only one example of continuum theories with internal constraints,
 55 i.e., constraints that, rather than being expressed through contact conditions between bodies, or
 56 through Dirichlet boundary conditions on one or more kinematic descriptors of a given body, restrict
 57 the admissibility of such descriptors in the internal points of the body itself. In fact, many other
 58 examples of internal constraints may be cited, which can be either holonomic or non-holonomic,
 59 and some of those have been reviewed by Capriz and Podio Guidugli [22] for “*oriented materials*”,
 60 and by Batra [18] and Carlson *et al.* [23] for thermo-elasticity and hyperelasticity, respectively.

61 In our opinion, it is important to emphasize that, in those theories mentioned above, in which
 62 the PVW is used to study materials with microstructure, the PVW is formulated by extending
 63 the kinematics of the “classical” continua² so as to include the structural degrees of freedom of

per unit volume [75].

²By “*classical*” *continua*, we mean continua that do not possess an *active* microstructure. For a continuum of this type, the microstructure, if at all considered, evolves *passively* under the action of either kinematic or dynamic entities, such as the deformation gradient tensor or Cauchy stress tensor, respectively, that are inherent to changes of configuration of the continuum under study. However, no specific micro-structural descriptor is introduced, be it viewed as an internal variable or as a representation of a structural degree of freedom. For example, fiber-reinforced materials can be studied as “classical” continua when the evolution of their microstructure, consisting in a reorientation of the fibers, is assumed to be a passive consequence of their deformation (see e.g. [44, 118] and the references therein). On the other hand, they can also be modeled as non-classical materials, when their microstructure is assumed to be active. In this case, the reorientation of the fibers is a dynamic process, coupled with the deformation, but virtually independent of it, that represents the manifestation of one or more micro-structural degrees of freedom [107]. One of these can be, for instance, the mean angle of the probability density distribution

64 the materials under study. Indeed, whereas the kinematics of a classical continuum is limited to
65 describe its motion in the three-dimensional Euclidean space, the extended kinematics describes
66 also the evolution of the microstructure of the continuum itself. In fact, this is achieved through the
67 introduction, for a given body, of suitable kinematic descriptors, which, along with their variations,
68 are virtually independent of the changes of shape of the body, and only have to be compatible with
69 the internal constraints that are possibly present.

70 The concept of extended kinematics is at the basis also of the theories of plasticity proposed
71 by Cermelli *et al.* [24], and Gurtin and Anand [71, 73], in which the Bilby-Kröner-Lee (BKL) de-
72 composition of the deformation gradient tensor is introduced, and the factor of such decomposition
73 termed *tensor of plastic distortions* is taken as the descriptor of the structural changes that, in
74 a body, are brought about by plasticity. In particular, Cermelli *et al.* [24] define stress-like gen-
75 eralized forces, which they call “*couple densities*”³, and study their balance under the constraint
76 of isochoric plastic distortions. Moreover, in the investigation of the dissipation inequality, they
77 compute the power that the “*couple densities*” produce on the rate of the tensor of plastic distor-
78 tions. In these respects, our approach has some similarities with the works by Cermelli *et al.* [24],
79 and Fried and Sellers [50], although, as discussed in detail below, our results are found within the
80 context of growth, and following a procedure explicitly based on a constrained version of the PVW
81 for the case of non-holonomic and rheonomic constraints, and on the use of the Lagrange multiplier
82 technique.

83 Within a line of thought similar to the one followed by Cermelli *et al.* [24], the idea of the
84 extended kinematics summarized above was adopted by DiCarlo and Quiligotti [38] in the context
85 of Biomechanics for addressing growth and remodeling. These processes are both anelastic, and
86 consist of the variation of mass and change of material properties of biological tissues [117] or cellular
87 complexes [49, 48, 110, 57, 35], respectively. In fact, in several biologically relevant situations, both
88 growth and remodeling are described by having recourse to the BKL decomposition [115], or to
89 similar decompositions (see e.g. [39]), and the factor of the decomposition employed that accounts
90 for the anelastic distortions accompanying growth or remodeling is sometimes referred to as *growth*
91 *tensor* or *remodeling tensor*. This tensor, thus, replaces the tensor of plastic distortions encountered
92 in elastoplasticity. Yet, a fundamental difference exists between plasticity and remodeling, on
93 the one side, and growth, on the other side. This difference is due to the fact that, whereas in
94 elastoplasticity and remodeling the tensor of inelastic distortions is often assumed to be isochoric
95 [116, 111], the growth tensor is required to comply with the mass balance law in the following
96 sense: the trace of a suitably defined rate of the growth tensor can be set equal to the normalized
97 source/sink of mass describing growth (see e.g. [41, 8, 97, 96]). The relation obtained this way
98 between the source/sink of mass and the growth tensor can be interpreted in different ways. In
99 particular, if the source/sink of mass is supplied from the outset, e.g. phenomenologically [8, 10,
100 100, 58], the relation in question amounts to translating the mass balance law into a *non-holonomic*
101 *and rheonomic constraint* on the growth tensor.

102 The just given interpretation of the mass balance constitutes the core of our present work. To
103 expand this idea, we first have to review some crucial points of the derivation outlined by DiCarlo

[16, 64, 67, 63, 31] that describes the orientation of the fibers in composite materials with statistical fiber distributions (see e.g. [88, 45, 93, 78] and the references therein.)

³A list of works that introduce generalized forces similar to the “*couple densities*” [24] and study the balance laws associated with them can be found in the work by Cermelli *et al.* [24], where these laws are called “*ancillary*”, and in the work by Fried and Sellers [50].

104 and Quiligotti [38], who base their approach to the mechanics of growth on the PVW. For their
105 purposes, indeed, they regard the growth tensor as the basic descriptor of the growth kinematics,
106 introduce the generalized virtual velocity associated with it, define a set of generalized forces dual to
107 the virtual velocity of the growth tensor, and obtain the balance of these forces as a consequence of
108 the localization of the integral equation expressing the PVW. We remark, however, that, although
109 DiCarlo and Quiligotti [38] speak of growth (and remodeling) in their paper, they do not mention
110 the mass balance law, nor do they discuss any *a priori* condition that the growth tensor should
111 fulfill, at least not explicitly. A review of their approach and its connection with the one presented
112 hereafter is the subject of a forthcoming work of ours.

113 Compared with the formulation summarized above, and with others that have come afterwards
114 (see e.g. [107]), we believe that the approach that we are proposing is novel because it treats
115 the mass balance law as a *non-holonomic and rheonomic constraint* on the growth tensor, and
116 provides a *constrained version* of the PVW relying on the Lagrange multiplier technique. More
117 specifically, by mimicking the PVW employed in computational mechanics for systems subjected to
118 internal constraints, as is the case, e.g., for incompressibility [79, 20], and adapting the procedure
119 to the non-holonomic and rheonomic case, we append the constraint on the growth tensor to the
120 “standard version” of the PVW [38] in order to determine the full set of equations that govern the
121 dynamics of the growing body under investigation. To the best of our knowledge, this procedure
122 is not standard for the case of non-holonomic and rheonomic constraints and, indeed, it has been
123 obtained by adapting some results put forward by Nadile [106] and Llibre *et al.* [95] in completely
124 different frameworks.

125 Although being conceived for the mechanics of volumetric growth, our results are meant to
126 apply to all those situations in which the kinematic variables describing the structural changes of
127 a body must satisfy one or more *a priori* conditions, dictated, for example, by the phenomenology
128 under study.

129 In our work, we also retrieve some results obtained by Gurtin [74], who provides a rational
130 derivation of the Cahn-Hilliard model for mass transport, and we reinterpret them in light of the
131 constrained version of the PVW within the context of growth mechanics. Our purpose, in this
132 case, is to show that, framed as we do in our approach, the formulation developed by Gurtin [74]
133 can be regarded as a “precursor” of a growth problem (although his paper, in fact, was published
134 two years later than the paper by Rodriguez *et al.* [115]). In this respect, our study aims to build
135 connections with other formulations of growth (see e.g. [41]) and to highlight both the similarities
136 and the conceptual differences among the considered approaches.

137 In order to give prominence to the theoretical results of our study, we prefer to show no numerical
138 simulations here, and to dedicate another work to the numerical aspects of our approach.

139 In our opinion, our analysis may contribute to construct a unified formulation of inelastic
140 processes, based on the paradigmatic procedure of the PVW, which is made compliant, when
141 necessary, with phenomenological laws treated as constraints.

142 2 General Notation

143 In this section, we briefly give the notation used throughout the rest of our work. To this end,
144 we introduce the three-dimensional Euclidean space \mathcal{S} , the reference placement of the body under
145 study, i.e., $\mathcal{B} \subset \mathcal{S}$, the time line \mathcal{I} , the time interval $[t_{\text{in}}, t_{\text{fin}}] \subset \mathcal{I}$, and the map $\chi(\cdot, t) : \mathcal{B} \rightarrow \mathcal{S}$,
146 which, for every time $t \in [t_{\text{in}}, t_{\text{fin}}] \subset \mathcal{I}$, transforms univocally each point X of \mathcal{B} into the point

147 $x = \chi(X, t) \in \mathcal{S}$, so that $\chi(\mathcal{B}, t) =: \mathcal{B}_t \subset \mathcal{S}$ represents the change of shape of the body from
 148 its reference placement to the placement \mathcal{B}_t attained at time t . Note that, with a slight abuse of
 149 terminology, we shall refer to this map simply as “motion” in the sequel. In addition, we define
 150 the auxiliary maps

$$\mathcal{X} : \mathcal{B} \times \mathcal{I} \rightarrow \mathcal{B}, \quad \mathcal{X}(X, t) = X, \quad (1a)$$

$$\mathcal{T} : \mathcal{B} \times \mathcal{I} \rightarrow \mathcal{I}, \quad \mathcal{T}(X, t) = t \quad (1b)$$

151 (see e.g. [46] and the references therein), which enjoy the properties

$$T\mathcal{X}(X, t) = \mathbf{I}(X, t), \quad \dot{\mathcal{X}}(X, t) = \mathbf{0}, \quad \forall (X, t) \in \mathcal{B} \times \mathcal{I}, \quad (2a)$$

$$\text{Grad}\mathcal{T}(X, t) = \mathbf{0}, \quad \dot{\mathcal{T}}(X, t) = 1, \quad \forall (X, t) \in \mathcal{B} \times \mathcal{I}, \quad (2b)$$

152 where $T\mathcal{X}(X, t)$ is the tangent map of $\mathcal{X}(\cdot, t)$ at $X \in \mathcal{B}$, $\mathbf{I}(X, t) : T_X\mathcal{B} \rightarrow T_X\mathcal{B}$ is the identity
 153 tensor, and $T_X\mathcal{B}$ is the tangent space of \mathcal{B} attached at $X \in \mathcal{B}$ (see e.g. [98]). For completeness,
 154 we also define the transpose of the identity tensor, i.e., $\mathbf{I}^\top(X, t) : T_X^*\mathcal{B} \rightarrow T_X^*\mathcal{B}$, with $T_X^*\mathcal{B}$ being
 155 the dual space of $T_X\mathcal{B}$, as well as the metric tensor associated with \mathcal{B} , i.e., $\mathbf{G}(X, t)$, for which it
 156 identically holds that $\dot{\mathbf{G}}(X, t) = \mathbf{0}$, for all $(X, t) \in \mathcal{B} \times \mathcal{I}$. By virtue of the maps χ and \mathcal{T} , any
 157 function $f : \mathcal{B}_t \times \mathcal{I} \rightarrow \mathbb{K}$, with \mathbb{K} representing the set of real numbers or any vector or tensor
 158 space, can be expressed as a function of the points of \mathcal{B} and time by means of the composition
 159 with the pair (χ, \mathcal{T}) , i.e., $f \circ (\chi, \mathcal{T}) : \mathcal{B} \times \mathcal{I} \rightarrow \mathbb{K}$, provided the composition makes sense.

160 Granted the usual differentiability properties of $\chi(\cdot, t)$, we introduce the deformation gradient
 161 tensor $\mathbf{F}(X, t) := T\chi(X, t) : T_X\mathcal{B} \rightarrow T_x\mathcal{S}$, where $T\chi(X, t)$ is the *tangent map* of $\chi(\cdot, t)$ at $X \in \mathcal{B}$,
 162 with $t \in [t_{\text{in}}, t_{\text{fin}}]$, while $T_x\mathcal{S}$ is the tangent space of \mathcal{S} attached at $x \equiv \chi(X, t) \in \mathcal{S}$ (see e.g. [98]).
 163 We also introduce the right Cauchy-Green deformation tensor $\mathbf{C}(X, t) := \mathbf{F}^\top(x, t)\mathbf{g}(x, t)\mathbf{F}(X, t)$,
 164 with $x \equiv \chi(X, t)$, and where $\mathbf{g}(x, t)$ is the metric tensor at $x \in \mathcal{S}$. It is understood that $\partial_t\mathbf{g}(x, t) =$
 165 $\mathbf{0}$, for all $x \in \mathcal{S}$ and $t \in \mathcal{I}$. We remark that $\mathbf{F}^\top(x, t)$ is defined as $\mathbf{F}^\top(x, t) : T_x^*\mathcal{S} \rightarrow T_X^*\mathcal{B}$,
 166 where $T_x^*\mathcal{S}$ is the dual space of $T_x\mathcal{S}$, and the notation $\mathbf{F}^\top \circ (\chi, \mathcal{T})$ should be used, when it is
 167 necessary to rephrase \mathbf{F}^\top as a function of the points of \mathcal{B} and time. However, when there it no
 168 room for confusion, to reduce the notational burden, we omit the composition with (χ, \mathcal{T}) , and
 169 tacitly redefine \mathbf{F}^\top as a function of the points of \mathcal{B} and time.

170 We recall the BKL decomposition, $\mathbf{F}(X, t) = \mathbf{F}_e(X, t)\mathbf{K}(X, t)$, where $\mathbf{F}_e(X, t)$ and $\mathbf{K}(X, t)$ are
 171 referred to as *tensor of elastic distortions* and *growth tensor*, respectively. The latter one, indeed,
 172 describes the anelastic distortions induced in the body by the variation of mass due to growth.
 173 For future use, we set $J := \det \mathbf{F}$, $J_e := \det \mathbf{F}_e$, and $J_{\mathbf{K}} := \det \mathbf{K}$. Here, we do not fuss over the
 174 physical meanings attributed to the BKL decomposition, since a huge literature is available on the
 175 topic (see e.g. [115, 117, 8, 38, 80, 51, 96, 6, 64, 19, 81, 86, 112, 65, 62, 114, 36, 5, 31]). However, we
 176 mention that, although \mathbf{K} is in principle a two-point tensor, in the sequel we consider it a mixed
 177 tensor from $T_X\mathcal{B}$ into a “relaxed” copy of this vector space (see e.g. [28, 36]).

178 Finally, the maps \mathcal{X} and \mathcal{T} defined in Equations (1a) and (1b) are useful to express the explicit
 179 dependence of physical quantities on the points of \mathcal{B} and time. For instance, if h is a physical
 180 quantity that can be written as $h(X, t) = \hat{h}(\mathbf{F}(X, t), \mathbf{K}(X, t), X, t)$, where \hat{h} is the constitutive
 181 representation of h , then the notation $h = \hat{h} \circ (\mathbf{F}, \mathbf{K}, \mathcal{X}, \mathcal{T})$ applies.

182 3 Mass balance as a constraint on the growth tensor

183 In this section, we briefly review the mass balance law of the body under study in the context of
 184 the theory of volumetric growth based on the BKL decomposition. To this end, we recall that such
 185 decomposition permits to rewrite the balance of mass of the considered body as a relation between
 186 the trace of the rate $\mathbf{K}^{-1}\dot{\mathbf{K}}$ and the normalized source/sink of mass R_γ , i.e. [41, 97, 9, 8],

$$\text{tr}(\mathbf{K}^{-1}\dot{\mathbf{K}}) \equiv \mathbf{K}^{-\text{T}} : \dot{\mathbf{K}} = R_\gamma, \quad \text{in } \mathcal{B} \times [t_{\text{in}}, t_{\text{fin}}], \quad (3)$$

187 where R_γ is defined as $R_\gamma := Jr_\gamma/\varrho_{\text{R}}$, r_γ is the “true” source/sink of mass, and ϱ_{R} is the mass
 188 density per unit volume of the body’s reference placement. Equation (3) is obtained from the mass
 189 balance law, expressed in local form and with respect to the reference placement of the body, i.e.,
 190 $\dot{\varrho}_{\text{R}} = Jr_\gamma$, by exploiting the relation $\varrho_{\text{R}} = J_{\mathbf{K}}\varrho_\nu$, where ϱ_ν is the mass density per unit volume of
 191 the body’s natural state, and using the identity $\dot{J}_{\mathbf{K}} = J_{\mathbf{K}}\text{tr}(\mathbf{K}^{-1}\dot{\mathbf{K}})$, under the hypothesis that ϱ_ν
 192 is constant in time.

193 We assume that R_γ is prescribed phenomenologically through a *growth law* of the type [100, 99]

$$R_\gamma \equiv R_{\gamma(\text{ph})} := \bar{R}_{\gamma(\text{ph})} \circ (\varphi, \omega) = \hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega), \quad \text{in } \mathcal{B} \times [t_{\text{in}}, t_{\text{fin}}], \quad (4)$$

194 where ω is the mass fraction of the nutrient substances (e.g. glucose or oxygen) that promote the
 195 accretion of the tissue’s mass, and $\varphi := -\frac{1}{3}\text{tr}\boldsymbol{\sigma}$ is the mechanical pressure in the tissue [100, 99],
 196 which, under suitable constitutive assumptions, can be expressed as $\varphi = \hat{\varphi} \circ (\mathbf{F}, \mathbf{K})$. As reported in
 197 [100, 99], the growth law (4) is calibrated in such a way that R_γ can be positive (mass accretion),
 198 null, or negative (mass resorption), depending on whether ω exceeds, equals, or goes below a certain
 199 threshold mass fraction, ω_{cr} . Finally, the dependence on φ is introduced since it is believed that
 200 pressure, when it is positive, has the capability of slowing down the rate of mass accretion [25],
 201 whereas it has no relevant influence on $R_{\gamma(\text{ph})}$, when it is negative.

202 To complete the description of $R_{\gamma(\text{ph})}$, the evolution of the nutrients’ mass fraction has to be
 203 described. This is done by taking into account the mass balance law of the nutrients. In this work,
 204 we assume that they are free to move within the body, and that such a motion can be modeled in
 205 terms of Fickian diffusion. In particular, it can be shown that, within the monophasic framework⁴,
 206 and written with respect to the reference placement of the body, the mass balance law of the
 207 nutrients becomes the diffusion-reaction equation, defined in $\mathcal{B} \times [t_{\text{in}}, t_{\text{fin}}]$, given by

$$J_{\mathbf{K}}\varrho_\nu\dot{\omega} - \text{Div}(J_{\mathbf{K}}\varrho_\nu\mathbf{D}\text{Grad}\omega) = -J_{\mathbf{K}}\varrho_\nu r_n\omega - J_{\mathbf{K}}\varrho_\nu[\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)]\omega, \quad (5)$$

208 where r_n is the rate at which the nutrients are absorbed by the tumor, and $\mathbf{D} := \hat{\mathbf{D}} \circ (\mathbf{F}, \mathbf{K})$ is the
 209 diffusivity tensor (see e.g. [15, 35] for possible constitutive expressions of \mathbf{D}). Moreover, following
 210 [8, 99, 36, 113], we can equip Equation (5) with boundary and initial conditions of the type

$$\omega = \omega_{\text{b}}, \quad \text{on } \partial_{\text{D}}^\omega \mathcal{B}, \quad (6a)$$

$$[-J_{\mathbf{K}}\varrho_\nu\mathbf{D}\text{Grad}\omega]\mathbf{N} = j_{\text{b}}, \quad \text{on } \partial_{\text{N}}^\omega \mathcal{B}, \quad (6b)$$

$$\omega(X, t_{\text{in}}) = \omega_{\text{in}}(X), \quad \text{in } \mathcal{B}, \quad (6c)$$

⁴For biological tissues and tumors, the monophasic framework is clearly much less descriptive than the biphasic, or the multiphasic, one [36, 69, 113]. However, it is sufficient for conveying the message contained in our work.

211 where ω_b and j_b are the nutrients' mass fraction and flux imposed on the Dirichlet portion $\partial_D^\omega \mathcal{B}$
 212 and on the Neumann portion $\partial_N^\omega \mathcal{B}$ of $\partial \mathcal{B}$ associated with ω , respectively.

213 Once $R_{\gamma(\text{ph})}$ is assigned from the outset, we regard Equation (3) as an *a priori* restriction on
 214 the rate $\dot{\mathbf{K}}$, for given \mathbf{F} , \mathbf{K} , and ω , and, accordingly, we rewrite it as

$$\hat{\mathcal{C}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \omega) := \mathbf{K}^{-\text{T}} : \dot{\mathbf{K}} - \hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega) = 0. \quad (7)$$

215 Equation (7) defines a *non-holonomic* and *rheonomic constraint* on \mathbf{K} (see e.g. [87] for a classi-
 216 fication of these constraints). The constraint is non-holonomic because it cannot be integrated,
 217 and, indeed, there exists no scalar function $f := \hat{f} \circ (\mathbf{F}, \mathbf{K}, \omega)$ whose time derivative coincides with
 218 $\hat{\mathcal{C}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \omega)$; it is rheonomic because $\hat{\mathcal{C}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \omega)$ depends on time not only through
 219 \mathbf{F} , \mathbf{K} and $\dot{\mathbf{K}}$, which are kinematic variables of the model, but also through ω , as prescribed by
 220 $\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)$.

221 **Remark 3.1 (More general form of the constraint $\hat{\mathcal{C}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \omega) = 0$)**

222 *The expression of the growth law and of the corresponding constraint can be made more general*
 223 *than the ones in Equations (4) and (7) by introducing a new function $\check{R}_{\gamma(\text{ph})}$, such that $R_{\gamma(\text{ph})} =$*
 224 *$\check{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \mathcal{X}, \mathcal{T})$, and the new function $\check{\mathcal{C}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \mathcal{X}, \mathcal{T})$, such that*

$$\check{\mathcal{C}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \mathcal{X}, \mathcal{T}) := \mathbf{K}^{-\text{T}} : \dot{\mathbf{K}} - \check{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \mathcal{X}, \mathcal{T}) = 0, \quad (8)$$

225 *where the composition with the maps \mathcal{X} and \mathcal{T} is meant to account for the explicit dependence of*
 226 *the growth law on material points and time virtually in all possible ways. A dependence of this*
 227 *type, for example, should be considered when an explicit expression of Equation (4) features mate-*
 228 *rial parameters that are functions of the material points and time, rather than being constants, as*
 229 *assumed later. According to Equation (8), the non-integrability of the constraint may be rephrased*
 230 *by saying that there exists no scalar function $f = \check{f} \circ (\mathbf{F}, \mathbf{K}, \mathcal{X}, \mathcal{T})$, whose time derivative co-*
 231 *incides with $\check{\mathcal{C}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \mathcal{X}, \mathcal{T})$. This is imputable to the functional form of the growth law*
 232 *$\check{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \mathcal{X}, \mathcal{T})$. We also mention that, within the framework of bone mechanics, there exist*
 233 *mathematical models of growth (see e.g. [90]) in which the growth law $R_{\gamma(\text{ph})}$ is given as a function*
 234 *of a biomechanical stimulus expressed through the convolution integral of the strain energy density*
 235 *of the material with a suitably defined kernel [90, 55].*

236 **Remark 3.2 (The limit case of holonomic, rheonomic constraint)**

237 *The constraint (8) turns out to be integrable if the growth law takes on the simple form $R_{\gamma} :=$*
 238 *$[R_{\gamma\text{p}} \circ \mathcal{X}][R_{\gamma\text{t}} \circ \mathcal{T}]$, where $R_{\gamma\text{p}}$ is a function of material points, and $R_{\gamma\text{t}}$ is a function of time that*
 239 *admits primitives in $[t_{\text{in}}, t_{\text{fin}}]$. Indeed, in this case, the constraint reads*

$$\check{\mathcal{C}}_{\mathbf{K}} \circ (\mathbf{K}, \dot{\mathbf{K}}, \mathcal{X}, \mathcal{T}) := \mathbf{K}^{-\text{T}} : \dot{\mathbf{K}} - [R_{\gamma\text{p}} \circ \mathcal{X}][R_{\gamma\text{t}} \circ \mathcal{T}] = 0, \quad (9)$$

240 *and it can be obtained by requiring the vanishing of the total time derivative of the function*

$$f := \check{f} \circ (\mathbf{K}, \mathcal{X}, \mathcal{T}) = \log \det \mathbf{K} - [R_{\gamma\text{p}} \circ \mathcal{X}][S_{\gamma\text{t}} \circ \mathcal{T}] + f_0 \circ \mathcal{X}, \quad (10)$$

241 *where $S_{\gamma\text{t}}$ is one primitive of $R_{\gamma\text{t}}$ over $[t_{\text{in}}, t_{\text{fin}}]$, i.e., $\dot{S}_{\gamma\text{t}}(t) = R_{\gamma\text{t}}(t)$ for $t \in [t_{\text{in}}, t_{\text{fin}}]$, and f_0 is*
 242 *an arbitrary function of material points, only. Accordingly, Equation (10) can be rephrased as*
 243 *a holonomic constraint that prescribes $\check{f} \circ (\mathbf{K}, \mathcal{X}, \mathcal{T})$ to remain constant in time over $[t_{\text{in}}, t_{\text{fin}}]$.*

244 Moreover, since, without loss of generality, the constant value of $\check{f} \circ (\mathbf{K}, \mathcal{X}, \mathcal{T})$ can be assumed to
 245 be zero, the constraint becomes

$$\check{f} \circ (\mathbf{K}, \mathcal{X}, \mathcal{T}) = 0 \quad \Rightarrow \quad \log \det \mathbf{K} - [R_{\gamma p} \circ \mathcal{X}][S_{\gamma t} \circ \mathcal{T}] = -f_0 \circ \mathcal{X}. \quad (11)$$

246 Finally, if $S_{\gamma t}$ is chosen as $S_{\gamma t}(t) := \int_{t_{\text{in}}}^t R_{\gamma t}(s) ds$, and the initial condition $\det \mathbf{K}(X, t_{\text{in}}) = 1$ is
 247 imposed, then, we achieve the identification $f_0(X) \equiv 0$, which yields

$$\det \mathbf{K}(X, t) \equiv J_{\mathbf{K}}(X, t) = \exp\left(R_{\gamma p}(X) \int_{t_{\text{in}}}^t R_{\gamma t}(s) ds\right), \quad \forall (X, t) \in \mathcal{B} \times [t_{\text{in}}, t_{\text{fin}}]. \quad (12)$$

248 Hence, the growth problem is reformulated as a problem subjected to an a priori condition on $\det \mathbf{K}$.
 249 This, in turn, could be understood as a “prescribed dilatation, or volumetric contraction, due to
 250 growth”, and features some similarities with the theory of swelling [120]. Moreover, if the growth
 251 law were switched off, the condition $\det \mathbf{K}(X, t) = 1$ would be obtained, thereby recovering isochoric
 252 inelastic distortions.

253 Before closing this section, we notice that, regardless of whether the constraint under study is
 254 expressed as in Equation (7) or as in Equation (8), a direct consequence of the introduction of the
 255 map \mathcal{T} (see Equations (1b) and (2b) for its properties) is that the constraint can be rewritten as
 256 a *Pfaffian form* [95], i.e., in terms of new functions that formally depend on the rate $\dot{\mathcal{T}}$ as follows

$$\hat{V}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \dot{\mathcal{T}}, \omega) := \mathbf{K}^{-\text{T}} : \dot{\mathbf{K}} - [\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)] \dot{\mathcal{T}} = 0, \quad (13a)$$

$$\check{V}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \dot{\mathcal{T}}, \mathcal{X}, \mathcal{T}) := \mathbf{K}^{-\text{T}} : \dot{\mathbf{K}} - [\check{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \mathcal{X}, \mathcal{T})] \dot{\mathcal{T}} = 0, \quad (13b)$$

257 where we have exploited Equation (2b).

258 4 Time as a constrained, fictitious Lagrangian parameter

259 To our knowledge, the non-holonomic and rheonomic nature of the constraint (7) presents some
 260 technical difficulties in the formulation of the Principle of Virtual Work (see e.g. [87]). Specifically,
 261 the main issue is that, when the method of Lagrange multipliers is invoked, the term $\hat{R}_{\gamma(\text{ph})} \circ$
 262 $(\mathbf{F}, \mathbf{K}, \omega)$ in Equation (7), or $\check{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \mathcal{X}, \mathcal{T})$ in Equation (8), cannot be combined, as it
 263 stands, with the virtual works expended on the virtual variations of χ and \mathbf{K} . This difficulty,
 264 however, can be circumvented by having recourse to an alternative formulation of the constraint,
 265 in which time is viewed as a *fictitious, additional Lagrangian parameter* of the considered problem.
 266 Before entering the details, we remark that this way of proceeding is not new *per se* (see e.g.
 267 [106, 95], and [87] for the case in which time is treated as an “ignorable variable”), and it can
 268 be put in our context on the basis of the rationale exposed in Appendix A1. Here, for the sake
 269 of conciseness, we say that the main reason for undertaking this path is to study the constraint
 270 expressed by Equation (7), or (8), within the setting of the Principle of Virtual Work. Indeed,
 271 regarding time as a Lagrangian parameter allows to introduce its virtual variations, along with a
 272 system of generalized, fictitious forces, dual to such variations and satisfying their own balance law.
 273 These forces produce virtual work against the virtual variations of time, and this virtual work can
 274 be combined with the work done on the same virtual variations by the term $\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)$, or

275 $\check{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \mathcal{X}, \mathcal{T})$, multiplied by a suitable Lagrange multiplier. A more detailed discussion on
 276 this topic is done below in this section as well as in the next one, and in Appendix A1.

277 For the purposes outlined above, in addition to \mathcal{T} in Equation (1b), we introduce

$$\mathfrak{T} : \mathcal{B} \times \mathcal{I} \rightarrow \mathcal{I}, \quad \mathfrak{T}(X, t) = t_X. \quad (14)$$

278 In principle, the auxiliary map \mathfrak{T} differs from \mathcal{T} in that the re-mapped time $t_X = \mathfrak{T}(X, t)$ is not *a*
 279 *priori* required to be equal to $t = \mathcal{T}(X, t)$, whereas the latter equality is true by definition.

280 To clarify the introduction of \mathfrak{T} , and its relation with \mathcal{T} , let us notice that, formally, \mathfrak{T} has
 281 the same “dignity” as χ and \mathbf{K} , and has the property of returning a unique instant of time
 282 $t_X = \mathfrak{T}(X, t) \in \mathcal{I}$, for each pair $(X, t) \in \mathcal{B} \times \mathcal{I}$, whereas $\chi(X, t) = x$ defines a unique position in
 283 space, and $\mathbf{K}(X, t)$ describes how the body elements of $T_X \mathcal{B}$ are relaxed at time $t \in \mathcal{I}$. Hence,
 284 while χ is a *space-like Lagrangian parameter*, and \mathbf{K} is a *structural Lagrangian parameter*, \mathfrak{T} could
 285 be termed *time-like Lagrangian parameter*, and, as a Lagrangian parameter of the theory, it can
 286 be associated with a dynamic equation [106]. Yet, \mathfrak{T} is fictitious, because its evolution is known
 287 *a priori* on physical grounds. Indeed, for consistency with the Galileian laws of composition of
 288 velocities and accelerations, \mathfrak{T} is restricted to produce, at most, the time translation

$$\mathfrak{T}(X, t) = \mathfrak{T}_0(X) + t = \mathfrak{T}_0(X) + \mathcal{T}(X, t) =: t_X \in \mathcal{I}, \quad \forall (X, t) \in \mathcal{B} \times \mathcal{I}, \quad (15)$$

289 where $\mathfrak{T}_0(X)$ is an arbitrary point-dependent time shift. In particular, Equation (15) guarantees
 290 the equality $\dot{\mathfrak{T}}(X, t) = 1$, for all $(X, t) \in \mathcal{B} \times \mathcal{I}$, which means that the “velocity of time” is equal
 291 to unity for all body points and for all times. Note that Equation (15) is a direct consequence of
 292 the fact that, in Galileian mechanics, *time is absolute*, since it is postulated to flow at the same
 293 rate for all observers. In fact, the equality $\dot{\mathfrak{T}}(X, t) = 1$ recasts Equation (15) in differential form,
 294 and can be interpreted as a *constraint* on \mathfrak{T} , or, better, on $\dot{\mathfrak{T}}$, which can be written as

$$\hat{\mathcal{V}}_{\dot{\mathfrak{T}}}(\dot{\mathfrak{T}}(X, t), \dot{\mathcal{T}}(X, t)) := \dot{\mathfrak{T}}(X, t) - \dot{\mathcal{T}}(X, t) = \dot{\mathfrak{T}}(X, t) - 1 = 0, \quad (16)$$

295 where $\hat{\mathcal{V}}_{\dot{\mathfrak{T}}} : \mathbb{R}^2 \rightarrow \mathbb{R}$ is defined by $\hat{\mathcal{V}}_{\dot{\mathfrak{T}}}(a_1, a_2) = a_1 - a_2 = 0$, for all $(a_1, a_2) \in \mathbb{R}^2$. Finally, by having
 296 recourse to the composition of maps, we obtain

$$\hat{\mathcal{V}}_{\dot{\mathfrak{T}}} \circ (\dot{\mathfrak{T}}, \dot{\mathcal{T}}) := \dot{\mathfrak{T}} - \dot{\mathcal{T}} = 0. \quad (17)$$

297 We denote by $T_t \mathcal{I}$ the one-dimensional tangent space of \mathcal{I} at t , and by $T\mathcal{I} := \sqcup_{t \in \mathcal{I}} T_t \mathcal{I}$ the
 298 tangent bundle of \mathcal{I} . Moreover, we define $\delta\mathcal{T} : \mathcal{B} \times \mathcal{I} \rightarrow T\mathcal{I}$ and $\delta\mathfrak{T} : \mathcal{B} \times \mathcal{I} \rightarrow T\mathcal{I}$ such that,
 299 for each $(X, t) \in \mathcal{B} \times \mathcal{I}$, $\delta\mathcal{T}(X, t) \in T_t \mathcal{I}$ and $\delta\mathfrak{T}(X, t) \in T_t \mathcal{I}$ represent a *virtual time translation*
 300 and the *virtual displacement associated with $\mathfrak{T}(X, t)$* , respectively. We notice that, since $\delta\mathfrak{T}(X, t)$ is
 301 defined as a virtual displacement, it has to be compatible with the imposed constraints, and, thus,
 302 it must satisfy Equations (16) and (17) in the form [95],

$$\hat{\mathcal{V}}_{\dot{\mathfrak{T}}}(\delta\mathfrak{T}(X, t), \delta\mathcal{T}(X, t)) = \delta\mathfrak{T}(X, t) - \delta\mathcal{T}(X, t) = 0, \quad \forall (X, t) \in \mathcal{B} \times \mathcal{I}, \quad (18a)$$

$$\hat{\mathcal{V}}_{\dot{\mathfrak{T}}} \circ (\delta\mathfrak{T}, \delta\mathcal{T}) = \delta\mathfrak{T} - \delta\mathcal{T} = 0. \quad (18b)$$

303 Before going further, we notice that the constraint in Equation (13a), and, equivalently in
 304 Equation (13b), is linear in the rates $\dot{\mathbf{K}}$ and $\dot{\mathcal{T}}$. Thus, by recalling the definition of $\delta\mathcal{T}$, and
 305 introducing the *virtual variation of the growth tensor* $\delta\mathbf{K} : \mathcal{B} \times \mathcal{I} \rightarrow [T\mathcal{B}]^1_1$, where $[T\mathcal{B}]^1_1$ is the

306 space of tensors mapping vectors of $T_X\mathcal{B}$ into vectors of $T_X\mathcal{B}$, we can rephrase Equation (13a)
 307 in the Lagrange-Chetaev form [95]⁵. This is obtained by replacing $\dot{\mathbf{K}}$ and $\dot{\mathcal{T}}$ with the “virtual
 308 displacements” $\delta\mathbf{K}$ and $\delta\mathcal{T}$, respectively, i.e.,

$$\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \delta\mathbf{K}, \delta\mathcal{T}, \omega) = \mathbf{K}^{-\text{T}} : \delta\mathbf{K} - [\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)]\delta\mathcal{T} = 0. \quad (19)$$

309 Moreover, Equations (17) and (18b) permit to rephrase the expressions of the constraint (13a) and
 310 (19) by substituting $\dot{\mathcal{T}}$ with $\dot{\mathfrak{T}}$ and $\delta\mathcal{T}$ with $\delta\mathfrak{T}$, thereby obtaining

$$\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \dot{\mathfrak{T}}, \omega) := \mathbf{K}^{-\text{T}} : \dot{\mathbf{K}} - [\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)]\dot{\mathfrak{T}} = 0, \quad (20a)$$

$$\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \delta\mathbf{K}, \delta\mathfrak{T}, \omega) = \mathbf{K}^{-\text{T}} : \delta\mathbf{K} - [\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)]\delta\mathfrak{T} = 0. \quad (20b)$$

311 Clearly, while the constraint expressed in Equation (20a) has physical dimensions of the recipro-
 312 cal of time, the one rewritten in Equation (19) is non-dimensional. However, these two versions can
 313 be made dimensionally coherent with each other by exploiting the fact that $\hat{\mathcal{V}}_{\mathbf{K}}$ is homogeneous of
 314 degree 1 in its third and fourth argument. Indeed, given a strictly positive constant $t_c > 0$, which
 315 may represent a characteristic time scale associated with the accretion or resorption of mass, it
 316 holds true that

$$\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, t_c\dot{\mathbf{K}}, t_c\dot{\mathfrak{T}}, \omega) = t_c[\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \dot{\mathfrak{T}}, \omega)] = 0, \quad (21)$$

317 which is equivalent to Equation (20a), and non-dimensional.

318 Similarly, although the constraint in Equation (18b) has physical dimensions of time, whereas
 319 that in Equation (17) is non-dimensional, we can write

$$\hat{\mathcal{V}}_{\mathfrak{T}} \circ (t_c\dot{\mathfrak{T}}, t_c\dot{\mathcal{T}}) = t_c[\hat{\mathcal{V}}_{\mathfrak{T}} \circ (\dot{\mathfrak{T}}, \dot{\mathcal{T}})] = 0, \quad (22)$$

320 thereby obtaining a constraint with the same physical dimensions as those in Equation (18b). We
 321 shall use this result in the constrained formulation of the Principle of Virtual Work.

322 **Remark 4.1 (The maps \mathfrak{T} and \mathcal{T})**

323 *A direct integration of Equation (17) with respect to time brings us back to Equation (15), in which*
 324 *$\mathfrak{T}_0(X)$ takes on the meaning of point-dependent integration constant. This can be particularized,*
 325 *for example, by requiring $\text{Grad } \mathfrak{T}(X, t) = \mathbf{0}$, for all $(X, t) \in \mathcal{B} \times \mathcal{I}$, so that the further condition*
 326 *$\text{Grad } \mathfrak{T}_0(X) = \mathbf{0}$ applies for all $X \in \mathcal{B}$. Thus, we can set $\mathfrak{T}(X, t) = t_X = t_0 + t$, with $t_0 := \mathfrak{T}_0(X)$*
 327 *being an arbitrary constant for all $X \in \mathcal{B}$, and, if we finally choose $t_0 = 0$, we obtain the unique*
 328 *solution $\mathfrak{T}(X, t) = t \equiv \mathcal{T}(X, t)$. However, in spite of this result, we find it convenient for the*
 329 *forthcoming discussion to maintain a conceptual distinction between \mathfrak{T} and \mathcal{T} . Indeed, whereas \mathfrak{T}*
 330 *is a (fictitious) Lagrangian parameter of the theory, constrained by Equation (17) to have unitary*
 331 *generalized velocity, \mathcal{T} is an auxiliary function that, through the composition of maps, is often*

⁵We say that a constraint is expressed in the “Lagrange-Chetaev form” if it can be written in a form in which the generalized virtual velocities involved in the constraint are replaced with the corresponding generalized displacements. In fact, this is possible, granted that the constraint complies with the Chetaev —or Lagrange-Chetaev— condition [95], in which case the constraint is also referred to as “ideal” [95]. By adapting the terminology used by Llibre et al. [95] to our context, the constraint $\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}, \dot{\mathfrak{T}}, \omega) = 0$ is ideal, since it is linear in the generalized velocities $\dot{\mathbf{K}}$ and $\dot{\mathfrak{T}}$, and, thus, it fulfills the Lagrange-Chetaev conditions, which reads $[\partial_{\dot{\mathbf{K}}} \hat{\mathcal{V}} \circ (\dots)] : \delta\mathbf{K} + [\partial_{\dot{\mathfrak{T}}} \hat{\mathcal{V}} \circ (\dots)]\delta\mathfrak{T} = \mathbf{K}^{-\text{T}} : \delta\mathbf{K} - [\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)]\delta\mathfrak{T} = 0$.

332 useful to express the explicit time dependence of some physical quantities in a formally correct way.
333 Above all, the main reason for distinguishing between \mathfrak{T} and \mathcal{T} is the one that has been anticipated
334 at the beginning of this section: since \mathfrak{T} is declared as a Lagrangian parameter, its virtual variation
335 $\delta\mathfrak{T}$ admits the introduction of fictitious forces, dual to $\delta\mathfrak{T}$, that produce virtual work on $\delta\mathfrak{T}$, and,
336 because of the identity $\delta\mathfrak{T} = \delta\mathcal{T}$, this virtual work can be added to the one done on $\delta\mathcal{T}$ by the
337 quantity $\mu_{\mathbf{K}}[\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)]$ or $\mu_{\mathbf{K}}[\check{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \mathcal{X}, \mathcal{T})]$, where $\mu_{\mathbf{K}}$ is the Lagrange multiplier
338 associated with the constraint (20a), put in the form (19) (see Equation (24a) below).

339 5 Principle of Virtual Work revisited

340 To account for the fact that the Principle of Virtual Work has to be written for arbitrary generalized
341 virtual displacements that are in harmony with the imposed constraints, we rephrase the PVW
342 formulated by DiCarlo and Quiligotti [38] for growth mechanics as explained below. First, we
343 recall that the kinematic descriptors of the present theory, which is of grade one in χ , and of grade
344 zero in \mathbf{K} [38] and \mathfrak{T} , are given by

$$(\chi, \mathbf{F}, \mathbf{K}, \mathfrak{T}, \delta\chi, \text{Grad}\delta\chi, \delta\mathbf{K}, \delta\mathfrak{T}). \quad (23)$$

345 Then, since we are going to append the constraints, both in the rescaled forms (21) and (22) and
346 in the Lagrange-Chetaev forms [95] (19) and (18b), to the expression of the PVW that one would
347 have in the absence of constraints, we introduce the Lagrange multipliers $\mu_{\mathbf{K}}$ and $\mu_{\mathfrak{T}}$, along with
348 their virtual variations $\delta\mu_{\mathbf{K}}$ and $\delta\mu_{\mathfrak{T}}$, so that the following duality pairings apply

$$\mu_{\mathbf{K}} \div [\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \delta\mathbf{K}, \delta\mathcal{T}, \omega)], \quad \mu_{\mathfrak{T}} \div [\hat{\mathcal{V}}_{\mathfrak{T}} \circ (\delta\mathfrak{T}, \delta\mathcal{T})], \quad (24a)$$

$$\delta\mu_{\mathbf{K}} \div [\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, t_c \dot{\mathbf{K}}, t_c \dot{\mathfrak{T}}, \omega)], \quad \delta\mu_{\mathfrak{T}} \div [\hat{\mathcal{V}}_{\mathfrak{T}} \circ (t_c \dot{\mathfrak{T}}, t_c \dot{\mathcal{T}})], \quad (24b)$$

349 where the symbol “ \div ” indicates the conjugation induced by duality.

350 By invoking duality again, we introduce the *internal generalized forces* that expend virtual work
351 on the virtual variations of the associated kinematic descriptors, i.e.,

$$\mathbf{P} \div \text{Grad}\delta\chi, \quad \mathbf{Y}_u \div \mathbf{K}^{-1}\delta\mathbf{K}, \quad \mathcal{Y}_u \div \delta\mathfrak{T}, \quad (25)$$

352 where \mathbf{P} is the “classical” first Piola-Kirchhoff stress tensor; \mathbf{Y}_u is referred to as *internal growth-*
353 *conjugated stress* in the sequel, since it is a stress-like quantity dual to $\mathbf{K}^{-1}\delta\mathbf{K}$; and \mathcal{Y}_u is termed
354 *internal time-conjugated force*, since it is dual to $\delta\mathfrak{T}$. The subscript “u” in \mathbf{Y}_u and \mathcal{Y}_u indicates
355 that these forces are “unconstrained”, in the sense that, because of the presence of the Lagrangian
356 multipliers $\mu_{\mathbf{K}}$ and $\mu_{\mathfrak{T}}$, they are associated with arbitrary (and, thus, “unconstrained”) variations
357 $\delta\mathbf{K}$ and $\delta\mathfrak{T}$, respectively.

358 Finally, we consider the external generalized forces

$$\mathbf{f}, \boldsymbol{\tau} \div \delta\chi, \quad \mathbf{Z} \div \mathbf{K}^{-1}\delta\mathbf{K}, \quad \mathcal{Z} \div \delta\mathfrak{T}, \quad (26)$$

359 where \mathbf{f} and $\boldsymbol{\tau}$ are the body forces per unit volume and the boundary contact forces per unit area
360 of “classical” Continuum Mechanics, respectively, while, from here on, \mathbf{Z} and \mathcal{Z} are said to be
361 *external growth-conjugated stress-like force*, and *external time-conjugated force*, respectively.

362 **Remark 5.1 (The external time-conjugated force \mathcal{Z})**

363 *The external time-conjugated force \mathcal{Z} is introduced by analogy with the external growth-conjugated*
 364 *stress-like force \mathbf{Z} . Indeed, as for \mathbf{Z} , whose origin has been discussed in [38, 37] for the case*
 365 *of growth, and that can be found also in [74, 24] for different problems, the rationale behind the*
 366 *introduction of \mathcal{Z} in our model is the one that has been anticipated at the beginning of the previous*
 367 *section as well as in Remark 4.1, and it can be summarized as follows. We admit that the definition*
 368 *of \mathfrak{T} as a Lagrangian parameter of the theory, and the definition of its virtual variation, i.e., $\delta\mathfrak{T}$,*
 369 *give room to the existence of forces dual to $\delta\mathfrak{T}$, which can be either internal or external, depending*
 370 *on the type of interaction that they model.*

371 With the premises outlined above, the constrained version of the PVW can be put in the form

$$\begin{aligned}
 & \int_{\mathcal{B}} \mathbf{P} : \text{Grad}\delta\chi + \int_{\mathcal{B}} \mathbf{Y}_u : \mathbf{K}^{-1}\delta\mathbf{K} + \int_{\mathcal{B}} \mathcal{Y}_u\delta\mathfrak{T} \\
 & + \int_{\mathcal{B}} \mu_{\mathbf{K}}[\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \delta\mathbf{K}, \delta\mathcal{T}, \omega)] + \int_{\mathcal{B}} \mu_{\mathfrak{T}}[\hat{\mathcal{V}}_{\mathfrak{T}} \circ (\delta\mathfrak{T}, \delta\mathcal{T})] \\
 & + \int_{\mathcal{B}} \delta\mu_{\mathbf{K}}[\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, t_c\dot{\mathbf{K}}, t_c\dot{\mathfrak{T}}, \omega)] + \int_{\mathcal{B}} \delta\mu_{\mathfrak{T}}[\hat{\mathcal{V}}_{\mathfrak{T}} \circ (t_c\dot{\mathfrak{T}}, t_c\dot{\mathcal{T}})] \\
 & = \int_{\mathcal{B}} \mathbf{f}\delta\chi + \int_{\partial_{\mathbf{N}}^{\mathbf{X}}\mathcal{B}} \boldsymbol{\tau}\delta\chi + \int_{\mathcal{B}} \mathbf{Z} : \mathbf{K}^{-1}\delta\mathbf{K} + \int_{\mathcal{B}} \mathcal{Z}\delta\mathfrak{T}, \tag{27}
 \end{aligned}$$

372 where $\partial\mathcal{B} = \partial_{\mathbf{N}}^{\mathbf{X}}\mathcal{B} \sqcup \partial_{\mathbf{D}}^{\mathbf{X}}\mathcal{B}$ is the boundary of \mathcal{B} , while $\partial_{\mathbf{N}}^{\mathbf{X}}\mathcal{B}$ and $\partial_{\mathbf{D}}^{\mathbf{X}}\mathcal{B}$ represent the Neumann and
 373 the Dirichlet portions of $\partial\mathcal{B}$, respectively. Clearly, since the four integrals featuring the constraints
 374 are identically zero, the PVW expressed in Equation (27) is only formally different from that of
 375 the unconstrained theory of growth put forward by DiCarlo and Quiligotti [38].

376 Before proceeding, it is worth mentioning that an approach similar to ours can be found in
 377 the context of the bone remodeling formulated under the assumption of “*optimal response*” [89].
 378 We also notice that, in the case of bone remodeling, the role that in our theory is played by the
 379 structural descriptor \mathbf{K} , is sometimes assigned to a scalar variable, termed “*microdeformation*”
 380 [55, 54], which is related to purely dissipative effects [30].

381 **5.1 Dynamic equations in local form**

382 By performing standard calculations, and writing explicitly $\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, \delta\mathbf{K}, \delta\mathcal{T}, \omega)$ and $\hat{\mathcal{V}}_{\mathfrak{T}} \circ$
 383 $(\delta\mathfrak{T}, \delta\mathcal{T})$, Equation (27) can be recast in the form

$$\begin{aligned}
 & \int_{\partial_{\mathbf{N}}^{\mathbf{X}}\mathcal{B}} \{\boldsymbol{\tau} - \mathbf{P}\mathbf{N}\}\delta\chi + \int_{\mathcal{B}} \{\text{Div}\mathbf{P} + \mathbf{f}\}\delta\chi \\
 & + \int_{\mathcal{B}} \{\mathbf{Z} - \mu_{\mathbf{K}}\mathbf{I}^{\text{T}} - \mathbf{Y}_u\} : \mathbf{K}^{-1}\delta\mathbf{K} + \int_{\mathcal{B}} \{\mathcal{Z} - \mathcal{Y}_u - \mu_{\mathfrak{T}}\}\delta\mathfrak{T} \\
 & + \int_{\mathcal{B}} \{\mu_{\mathbf{K}}[\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)] + \mu_{\mathfrak{T}}\}\delta\mathcal{T} \\
 & - \int_{\mathcal{B}} \delta\mu_{\mathbf{K}}[\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, t_c\dot{\mathbf{K}}, t_c\dot{\mathfrak{T}}, \omega)] - \int_{\mathcal{B}} \delta\mu_{\mathfrak{T}}[\hat{\mathcal{V}}_{\mathfrak{T}} \circ (t_c\dot{\mathfrak{T}}, t_c\dot{\mathcal{T}})] = 0, \tag{28}
 \end{aligned}$$

384 which has to hold true for arbitrary $\delta\chi$ vanishing on $\partial_D^x\mathcal{B}$, and for arbitrary $\delta\mathbf{K}$, $\delta\mathfrak{T}$, $\delta\mathcal{T}$, $\delta\mu_{\mathbf{K}}$, and
385 $\delta\mu_{\mathfrak{T}}$. Moreover, localizing Equation (28), and appending the Dirichlet condition for χ on $\partial_D^x\mathcal{B}$ lead
386 to the *mixed formulation*

$$\text{Div}\mathbf{P} + \mathbf{f} = \mathbf{0}, \quad \text{in } \mathcal{B}, \quad (29a)$$

$$\chi = \chi_b, \quad \text{on } \partial_D^x\mathcal{B}, \quad (29b)$$

$$\mathbf{P}\mathbf{N} = \boldsymbol{\tau}, \quad \text{on } \partial_N^x\mathcal{B}, \quad (29c)$$

$$(\mathbf{Y}_u + \mu_{\mathbf{K}}\mathbf{I}^T) - \mathbf{Z} = \mathbf{0}, \quad \text{in } \mathcal{B}, \quad (29d)$$

$$(\mathcal{Y}_u + \mu_{\mathfrak{T}}) - \mathcal{Z} = 0, \quad \text{in } \mathcal{B}, \quad (29e)$$

$$\mu_{\mathbf{K}}[\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)] + \mu_{\mathfrak{T}} = 0, \quad \text{in } \mathcal{B}, \quad (29f)$$

$$\hat{\mathcal{V}}_{\mathbf{K}} \circ (\mathbf{F}, \mathbf{K}, t_c \dot{\mathbf{K}}, t_c \dot{\mathfrak{T}}, \omega) = 0, \quad \text{in } \mathcal{B}, \quad (29g)$$

$$\hat{\mathcal{V}}_{\mathfrak{T}} \circ (t_c \dot{\mathfrak{T}}, t_c \dot{\mathcal{T}}) = 0, \quad \text{in } \mathcal{B}. \quad (29h)$$

387 Equation (29a) is the local form of the balance of linear momentum of “classical” Continuum
388 Mechanics, equipped with the Dirichlet boundary condition (29b) and the Neumann boundary
389 condition (29c), where χ_b is the motion prescribed on $\partial_D^x\mathcal{B}$, and \mathbf{N} is the field of co-normals
390 defined over $\partial\mathcal{B}$.

391 Equation (29d) is equivalent to the balance of the growth-conjugated stress-like generalized
392 forces that was obtained by DiCarlo and Quiligotti [38] in their picture of growth mechanics,
393 provided the identification $\mathbf{Y} \equiv \mathbf{Y}_u + \mu_{\mathbf{K}}\mathbf{I}^T$ is made, where \mathbf{Y} denotes the *overall, internal, growth-*
394 *conjugated stress* dual to $\mathbf{K}^{-1}\delta\mathbf{K}$ (see also [24] for a similar force balance obtained in the context
395 of plasticity), and corresponds to what DiCarlo and Quiligotti [38] indicate with “-C” and call
396 “*remodelling self-couple*”. Clearly, our external force \mathbf{Z} corresponds to the external “*remodelling*
397 *couple*” denoted by “B” by DiCarlo and Quiligotti [38]. In this respect, we notice that, apart
398 from having re-defined \mathbf{Y} as the sum of its unconstrained part, i.e., \mathbf{Y}_u , and the part given by the
399 Lagrange multiplier, i.e., $\mu_{\mathbf{K}}\mathbf{I}^T$, Equation (29d) is not new and, in fact, it is rather well-established
400 in several papers on inelastic processes (see e.g. [76, 24, 38, 77, 72, 37, 7, 107, 6, 12, 64, 105, 66, 31,
401 5, 69, 27, 26]). However, a novelty of our approach is that we are viewing growth as a constrained
402 problem, as testified by the presence of the Lagrange multiplier $\mu_{\mathbf{K}}$ in $\mathbf{Y} \equiv \mathbf{Y}_u + \mu_{\mathbf{K}}\mathbf{I}^T$. To this
403 end, a constitutive law relating \mathbf{Y}_u to $\dot{\mathbf{K}}$ will be sought for and, consequently, Equation (29d) will
404 be turned into an ordinary differential equation in \mathbf{K} , and solved with respect to this tensorial
405 variable.

406 Equation (29e) defines the balance of the generalized forces dual to $\delta\mathfrak{T}$, for which, in analogy
407 with Equation (29d), one can identify $\mathcal{Y} \equiv \mathcal{Y}_u + \mu_{\mathfrak{T}}$. Equation (29f), instead, defines a balance
408 between the Lagrange multipliers of the theory. We emphasize that, in spite of the fact that
409 Equation (29e) has the same structure as Equation (29d), it has a different meaning. Indeed,
410 since the evolution of the fictitious Lagrangian parameter \mathfrak{T} is entirely described by the constraint
411 (29h), which yields $\mathfrak{T}(X, t) = t$, for all $(X, t) \in \mathcal{B} \times \mathcal{I}$ (see also the discussion in Remark 4.1),
412 Equation (29e) determines the difference $\mathcal{Z} - \mathcal{Y}_u$ [106]. In this respect, we highlight that Equations
413 (29e) and (29f) are new in the theory of volumetric growth, at least to the best of our knowledge.
414 However, similar equations were obtained by Nadile [106] in a completely different context. Finally,
415 Equations (29g) and (29h) return the constraints.

416 After the constitutive framework is established, Equations (29a) and (29d)–(29h) constitute a
417 set of 16 scalar equations in the unknowns χ , \mathbf{K} , $\mu_{\mathbf{K}}$, $\mu_{\mathfrak{T}}$, $\mathcal{Z} - \mathcal{Y}_u$, and \mathfrak{T} , which amount to 16 scalar

418 unknowns. Hence, the problem is closed. In particular, Equation (29g) allows to determine the
 419 Lagrange multiplier $\mu_{\mathbf{K}}$ (although, given the specific hypotheses adopted in this work, a different
 420 procedure will be used in the sequel), while Equation (29h) is used to obtain $\mathfrak{T}(X, t) = t$, so that the
 421 Lagrange multiplier $\mu_{\bar{\mathfrak{T}}}$ is determined by means of Equation (29f). In our opinion, the constraint
 422 on time constitutes a novelty in our approach, since it has not been considered in the previous
 423 formulations of growth which we are aware of.

424 5.2 Preparation of the initial and boundary value problem (IBVP)

425 After substituting the explicit expressions of the constraints (17) and (20a) into Equations (29h)
 426 and (29g), respectively, and dropping the strictly positive constant t_c featuring in these equations,
 427 we proceed with the solution of the system (29a)–(29h).

428 First, we notice that Equations (29e) and (29f) can be decoupled from the other ones and
 429 rewritten as

$$\mathcal{Y}_u + \mu_{\bar{\mathfrak{T}}} = \mathcal{Z}, \quad \text{in } \mathcal{B}, \quad (30a)$$

$$\mu_{\bar{\mathfrak{T}}} = -\mu_{\mathbf{K}}[\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)], \quad \text{in } \mathcal{B}, \quad (30b)$$

430 so that the Lagrange multiplier $\mu_{\bar{\mathfrak{T}}}$ can be determined by the right-hand-side of Equation (30b),
 431 once $\mu_{\mathbf{K}}$ is known. Accordingly, Equation (30a) becomes

$$\mathcal{Z} - \mathcal{Y}_u = \mu_{\bar{\mathfrak{T}}} = -\mu_{\mathbf{K}}[\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)], \quad \text{in } \mathcal{B}. \quad (31)$$

432 Second, Equations (29d) and (29g) can be studied separately from the other ones, so that one
 433 obtains

$$\mathbf{Y}_u + \mu_{\mathbf{K}} \mathbf{I}^T - \mathbf{Z} = \mathbf{0}, \quad \text{in } \mathcal{B}, \quad (32a)$$

$$\mathbf{K}^{-T} : \dot{\mathbf{K}} - \hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega) = 0, \quad \text{in } \mathcal{B}. \quad (32b)$$

434 Consequently, $\mu_{\mathbf{K}}$ can be computed by separating the spherical part of Equation (32a) from its
 435 deviatoric counterpart, so that Equations (32a) and (32b) become

$$\text{dev} \mathbf{Y}_u = \text{dev} \mathbf{Z}, \quad \text{in } \mathcal{B}, \quad (33a)$$

$$\mathbf{K}^{-T} : \dot{\mathbf{K}} = \hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega), \quad \text{in } \mathcal{B}, \quad (33b)$$

$$\mu_{\mathbf{K}} = \frac{1}{3} \text{tr} \mathbf{Z} - \frac{1}{3} \text{tr} \mathbf{Y}_u, \quad \text{in } \mathcal{B}. \quad (33c)$$

436 Now, if \mathbf{Z} is supplied through a function independent of $\dot{\mathbf{K}}$ and other time derivatives of \mathbf{K} of
 437 order higher than the first, and if \mathbf{Y}_u is expressed constitutively as a function of \mathbf{K} and $\dot{\mathbf{K}}$, then
 438 Equations (33a) and (33b) become a set of first-order ordinary differential equations. Thus, once
 439 \mathbf{Z} is assigned and \mathbf{Y}_u is provided constitutively, the Lagrangian multiplier $\mu_{\mathbf{K}}$ is determined by
 440 the right-hand-side of Equation (33c), while Equations (33a) and (33b) are sufficient to determine
 441 the 9 independent components of \mathbf{K} . Therefore, the boundary value problem that has to be solved

442 according to the formulation presented in this work is given by

$$\operatorname{Div} \mathbf{P} + \mathbf{f} = \mathbf{0}, \quad \text{in } \mathcal{B}, \quad (34a)$$

$$\chi = \chi_b, \quad \text{on } \partial_D^X \mathcal{B}, \quad (34b)$$

$$\mathbf{P} \mathbf{N} = \boldsymbol{\tau}, \quad \text{on } \partial_N^X \mathcal{B}, \quad (34c)$$

$$\operatorname{dev} \mathbf{Y}_u = \operatorname{dev} \mathbf{Z}, \quad \text{in } \mathcal{B}, \quad (34d)$$

$$\mathbf{K}^{-T} : \dot{\mathbf{K}} = \hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega), \quad \text{in } \mathcal{B}, \quad (34e)$$

443 which, apart from the boundary conditions (34b) and (34c), involves 12 independent equations in
 444 12 unknowns (3 equations for χ and 9 equations for \mathbf{K}), while $\mu_{\mathbf{K}}$, $\mu_{\bar{\chi}}$, and $\mathcal{Z} - \mathcal{Y}_u$ can be computed
 445 *a posteriori* by means of Equations (33c), (30b), and (31). To do that, it is necessary to supply \mathbf{P}
 446 and \mathbf{Y}_u constitutively.

447 6 Constitutive laws and final form of the initial and boundary 448 value problem

449 Given for granted that the constitutive expressions for \mathbf{P} and \mathbf{Y}_u comply with all the axioms of
 450 the theory of constitutive laws, we focus here on their thermodynamical admissibility. To this end,
 451 we adhere to the framework presented by Gurtin [74], which we slightly adapt to our purposes,
 452 and, in the following study of the dissipation inequality, we consider the limit case in which \mathcal{Z} is
 453 assumed to vanish from the outset. However, in Appendix A2, we study the opposite point of view,
 454 in which \mathcal{Z} is *not* assumed to be zero, and is rather regarded as an unknown of the model. Hence,
 455 by taking inspiration from [24, 74, 75] for the general structure of the dissipation associated with
 456 a fixed region $\mathcal{R} \subset \mathcal{B}$, we write here

$$\int_{\mathcal{R}} \mathcal{D}_R = - \int_{\mathcal{R}} \dot{\Psi}_R + \underbrace{\int_{\mathcal{R}} \mathbf{f} \mathbf{v} + \int_{\partial \mathcal{R}} (\mathbf{P} \mathbf{N}) \mathbf{v}}_{\mathcal{P}_{\text{ext}}^{(\text{net}, \chi)}} + \underbrace{\int_{\mathcal{R}} \mathbf{Z} : \mathbf{K}^{-1} \dot{\mathbf{K}}}_{\mathcal{P}_{\text{ext}}^{(\text{net}, \mathbf{K})}} + \underbrace{\int_{\mathcal{R}} \mu_{\text{ch}} [\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)]}_{\mathcal{M}_{\text{ext}}} \geq 0, \quad (35)$$

457 and refer to Gurtin [74] for an explanation of the fifth term on the right-hand-side of Equation
 458 (35) (see Remark 6.1). We emphasize that, within the theoretical framework presented in this
 459 section, one cannot expect to obtain \mathcal{Y}_u through the study of Equation (35). Indeed, the force \mathcal{Y}_u
 460 determined below follows directly from the force balance (31) under the simplifying assumption of
 461 vanishing \mathcal{Z} . A different approach, in which \mathcal{Y}_u is determined constitutively and \mathcal{Z} solves the force
 462 balance (31) is shown in Appendix A2.

463 In Equation (35), \mathcal{D}_R and Ψ_R are the dissipation density and Helmholtz free energy density per
 464 unit volume of the reference placement, respectively, $\mathcal{P}_{\text{ext}}^{(\text{net}, \chi)}$ is the external net power [24] associated
 465 with the Lagrangian parameter χ through the velocity $\mathbf{v} := \dot{\chi}$; $\mathcal{P}_{\text{ext}}^{(\text{net}, \mathbf{K})}$ denotes the external net
 466 power conjugated with $\mathbf{K}^{-1} \dot{\mathbf{K}}$, and μ_{ch} is identified with a generalized *chemical potential*, whose
 467 product with the growth law $R_{\gamma(\text{ph})} \equiv \hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)$ defines \mathcal{M}_{ext} , i.e., in a modified version
 468 of Gurtin's words [74], the power that is added to or subtracted from the system by means of the
 469 addition (when $R_{\gamma(\text{ph})} > 0$) or depletion of mass (when $R_{\gamma(\text{ph})} < 0$).

470 **Remark 6.1 (On the presence of \mathcal{M}_{ext} in Equation (35))**

471 *In his expression of the dissipation inequality, Gurtin [74] introduces the term that we have denoted*
 472 *here by \mathcal{M}_{ext} because, in his model, the mass source is declared as an entity that operates on*
 473 *the system that he considers from the world outside it [74]. Indeed, in analogy with the external*
 474 *powers $\mathcal{P}_{\text{ext}}^{(\text{net},\chi)}$ and $\mathcal{P}_{\text{ext}}^{(\text{net},\mathbf{K})}$, the term \mathcal{M}_{ext} must feature explicitly in the dissipation inequality,*
 475 *since it constitutes the external power due to the transport of mass. As such, and as anticipated*
 476 *above, it is represented by the action of the generalized force dual to the variation of mass, i.e., the*
 477 *chemical potential μ_{ch} , on the mass source/sink, which is the conjugated generalized rate. Within*
 478 *our approach, the mass source/sink is given phenomenologically from the outset, and is thus regarded*
 479 *as external, thereby making our formulation similar to the one presented by Gurtin [74]. This*
 480 *concept is explained also by Fried and Sellers [50], although they investigate a different situation.*
 481 *Indeed, also other approaches are possible. In fact, Fried and Sellers [50] elaborate a model in which*
 482 *their source/sink of mass is introduced as a supply/loss of mass operating from the inside of the*
 483 *system under study. Consistently with this point of view, their source/sink of mass cannot feature*
 484 *explicitly in the definition of the dissipation inequality, although it can be made to appear in the*
 485 *subsequent expression of the dissipation obtained by exploiting the mass balance law. This difference*
 486 *between the approach proposed by Gurtin [74], and slightly modified in our work, and the approach*
 487 *proposed by Fried and Sellers [50] is, in fact, essential. Indeed, since Fried and Sellers [50] treat*
 488 *the mass source/sink as an internal constitutive variable, they have to determine a constitutive law*
 489 *for it.*

490 6.1 Local dissipation

491 We proceed with the localization of the dissipation inequality (35) under the assumption that
 492 $\mathcal{R} \subset \mathcal{B}$ is independent of time [24]. To this end, we apply Gauss' Theorem, and enforce the
 493 dynamic equations (29a) and (29d), thereby obtaining

$$\mathcal{D}_{\text{R}} = -\dot{\Psi}_{\text{R}} + \mathbf{P} : \dot{\mathbf{F}} + (\mathbf{Y}_{\text{u}} + \mu_{\mathbf{K}} \mathbf{I}^{\text{T}}) : \mathbf{K}^{-1} \dot{\mathbf{K}} + \mu_{\text{ch}} [\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)] \geq 0. \quad (36)$$

494 By recalling Equation (7), which implies $\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega) = \mathbf{I}^{\text{T}} : \mathbf{K}^{-1} \dot{\mathbf{K}}$, Equation (36) features
 495 the term $(\mu_{\mathbf{K}} + \mu_{\text{ch}}) [\mathbf{I}^{\text{T}} : \mathbf{K}^{-1} \dot{\mathbf{K}}]$, which can be eliminated by setting $\mu_{\text{ch}} = -\mu_{\mathbf{K}}$, thereby obtaining

$$\mathcal{D}_{\text{R}} = -\dot{\Psi}_{\text{R}} + \mathbf{P} : \dot{\mathbf{F}} + \mathbf{Y}_{\text{u}} : \mathbf{K}^{-1} \dot{\mathbf{K}} \geq 0. \quad (37)$$

496 To study Equation (37), we write Ψ_{R} as $\Psi_{\text{R}} = J_{\mathbf{K}} \Psi_{\nu}$, where Ψ_{ν} is the body's Helmholtz free
 497 energy density per unit volume of the natural state, and, under the hypothesis of hyperelastic
 498 material, we express Ψ_{ν} constitutively as $\Psi_{\nu} = \hat{\Psi}_{\nu} \circ (\mathbf{F} \mathbf{K}^{-1})$, so that Ψ_{R} can be re-defined as
 499 $\Psi_{\text{R}} = \hat{\Psi}_{\text{R}} \circ (\mathbf{F}, \mathbf{K}) = J_{\mathbf{K}} [\hat{\Psi}_{\nu} \circ (\mathbf{F} \mathbf{K}^{-1})]$. Then, by computing the time derivative of Ψ_{R} , substituting
 500 it into Equation (37), and making the identifications

$$\mathbf{P} = \hat{\mathbf{P}} \circ (\mathbf{F}, \mathbf{K}) = \frac{\partial \hat{\Psi}_{\text{R}}}{\partial \mathbf{F}} \circ (\mathbf{F}, \mathbf{K}) = (\det \mathbf{K}) \left(\frac{\partial \hat{\Psi}_{\nu}}{\partial \mathbf{F} \mathbf{K}^{-1}} \circ (\mathbf{F} \mathbf{K}^{-1}) \right) \mathbf{K}^{-\text{T}}, \quad (38\text{a})$$

$$\mathbf{H} = \hat{\mathbf{H}} \circ (\mathbf{F}, \mathbf{K}) = \mathbf{K}^{\text{T}} \left(\frac{\partial \hat{\Psi}_{\text{R}}}{\partial \mathbf{K}} \circ (\mathbf{F}, \mathbf{K}) \right) = [\hat{\Psi}_{\text{R}} \circ (\mathbf{F}, \mathbf{K})] \mathbf{I}^{\text{T}} - \mathbf{F}^{\text{T}} [\hat{\mathbf{P}} \circ (\mathbf{F}, \mathbf{K})], \quad (38\text{b})$$

$$\mathbf{Y}_{\text{u,d}} := \mathbf{Y}_{\text{u}} - [\hat{\mathbf{H}} \circ (\mathbf{F}, \mathbf{K})], \quad (38\text{c})$$

501 where \mathbf{H} is Eshelby stress tensor, and $\mathbf{Y}_{u,d}$ is the *dissipative part* of \mathbf{Y}_u (see also [24, 38, 37]), the
 502 dissipation inequality reduces to

$$\mathcal{D}_R = \mathbf{Y}_{u,d} : \mathbf{K}^{-1} \dot{\mathbf{K}} \geq 0. \quad (39)$$

503 6.2 Constitutive laws

504 By looking at Equation (39), and restricting our study to the linear theory and to the isotropic
 505 case, we express $\mathbf{Y}_{u,d}$ by using a decomposition of fourth-order tensors [108] that yields (see also
 506 [70, 64, 94])

$$\begin{aligned} \mathbf{Y}_{u,d} &:= \hat{\mathbf{Y}}_{u,d} \circ (\mathbf{F}, \mathbf{K}, \dot{\mathbf{K}}) = \frac{1}{3} J_{\mathbf{K}} \mathbf{a}_\nu \text{tr}(\mathbf{K}^{-1} \dot{\mathbf{K}}) \mathbf{I}^T + J_{\mathbf{K}} \mathbf{b}_\nu \{ \mathbf{C} \mathbf{K}^{-1} \dot{\mathbf{K}} \mathbf{C}^{-1} + (\mathbf{K}^{-1} \dot{\mathbf{K}})^T \} \\ &\quad + J_{\mathbf{K}} \mathbf{c}_\nu \{ \mathbf{C} \mathbf{K}^{-1} \dot{\mathbf{K}} \mathbf{C}^{-1} - (\mathbf{K}^{-1} \dot{\mathbf{K}})^T \} \\ &= [\hat{\mathbb{T}} \circ (\mathbf{F}, \mathbf{K})] : (\mathbf{K}^{-1} \dot{\mathbf{K}}), \end{aligned} \quad (40)$$

507 where \mathbf{a}_ν , \mathbf{b}_ν , and \mathbf{c}_ν are constant material parameters such that $\mathbf{a}_\nu + 2\mathbf{b}_\nu \geq 0$, $\mathbf{b}_\nu \geq 0$, and $\mathbf{c}_\nu \geq 0$,
 508 while $\hat{\mathbb{T}} \circ (\mathbf{F}, \mathbf{K})$ is the constitutive function, mapped in the space of fourth-order tensors, given by

$$\hat{\mathbb{T}} \circ (\mathbf{F}, \mathbf{K}) := \frac{1}{3} J_{\mathbf{K}} \mathbf{a}_\nu \mathbf{I}^T \otimes \mathbf{I}^T + J_{\mathbf{K}} \mathbf{b}_\nu \{ \mathbf{C} \underline{\otimes} \mathbf{C}^{-1} + \mathbf{I}^T \bar{\otimes} \mathbf{I} \} + J_{\mathbf{K}} \mathbf{c}_\nu \{ \mathbf{C} \underline{\otimes} \mathbf{C}^{-1} - \mathbf{I}^T \bar{\otimes} \mathbf{I} \}. \quad (41)$$

509 Next, we discuss the external forces \mathbf{f} and \mathbf{Z} . Whereas \mathbf{f} is often assumed to be negligible in
 510 the mechanics of tumor growth, \mathbf{Z} may be important in the evolution of a tumor [37]. To us, this
 511 generalized force may be the expression of genetic and/or epigenetic and/or chemical information,
 512 appropriately “translated” into mechanical interactions (cf. the interpretation given by [37]). In our
 513 opinion, providing accurate models of such interactions is not straightforward and further research
 514 in this direction is therefore necessary. In an ongoing work of ours, we propose a possible expression
 515 for \mathbf{Z} on the basis of several discussions with colleagues and former co-workers⁶. However, since
 516 providing an explicit expression for \mathbf{Z} is not the focus of the present work, we simply assume here
 517 that it can be assigned as $\mathbf{Z} := \hat{\mathbf{Z}} \circ (\mathbf{F}, \mathbf{K}, \omega, \text{Grad } \omega)$. In particular, we choose \mathbf{Z} such that $\mathbf{C}^{-1} \mathbf{Z}$,
 518 and, thus, also $\mathbf{C}^{-1} \text{dev} \mathbf{Z}$, are symmetric second-order tensor fields, so that, according to Equation
 519 (34d), $\mathbf{C}^{-1} \text{dev} \mathbf{Y}_u$ is symmetric, too. Consequently, the term multiplied by the generalized viscosity
 520 \mathbf{c}_ν in Equation (40) has to be zero.

521 6.3 Final form of the IBVP

522 In summary, the set of equations describing the considered growing medium consists of Equation
 523 (34a), i.e., the linear momentum balance law, which determines the medium’s deformation, χ ;
 524 Equations (34d), i.e., the balance of forces dual to the unconstrained part of $\dot{\mathbf{K}}$; Equation (34e),
 525 i.e., the constraint describing the medium’s growth; Equation (5), which represents the diffusion-
 526 reaction equation for the nutrients’ mass fraction, ω . The above mentioned list of equations is
 527 equipped with the boundary conditions (34b) and (34c), assessing prescribed deformations and
 528 tractions, and with the boundary conditions (6a) and (6b) assigned on ω . Analogously, we prescribe

⁶We acknowledge, in particular, several discussions done with Ms. Francesca Ballatore and especially with Ms. Valentina Licari at the time of her Master of Science thesis [94].

529 an initial condition of the type $\mathbf{K}(X, t_{\text{in}}) = \mathbf{K}_{\text{in}}(X)$ for the growth tensor and the initial condition
 530 for ω expressed in Equation (6c). Finally, we obtain the IBVP

$$\text{Div} \mathbf{P} = -\mathbf{f}, \quad \text{in } \mathcal{B}, \quad (42a)$$

$$\chi = \chi_{\text{b}}, \quad \text{on } \partial_{\text{D}}^{\chi} \mathcal{B}, \quad (42b)$$

$$\mathbf{P} \mathbf{N} = \boldsymbol{\tau}, \quad \text{on } \partial_{\text{N}}^{\chi} \mathcal{B}, \quad (42c)$$

$$2J_{\mathbf{K}} \mathbf{b}_{\nu} \text{dev}_{\mathbf{C}} \text{sym}[(\mathbf{K}^{-1} \dot{\mathbf{K}}) \mathbf{C}^{-1}] = -\mathbf{C}^{-1} \text{dev} \mathbf{H} + \mathbf{C}^{-1} \text{dev} \mathbf{Z}, \quad \text{in } \mathcal{B}, \quad (42d)$$

$$2J_{\mathbf{K}} \mathbf{c}_{\nu} \text{skew}[(\mathbf{K}^{-1} \dot{\mathbf{K}}) \mathbf{C}^{-1}] = \mathbf{0}, \quad \text{in } \mathcal{B}, \quad (42e)$$

$$\mathbf{K}^{-\text{T}} : \dot{\mathbf{K}} = R_{\gamma(\text{ph})}, \quad \text{in } \mathcal{B}, \quad (42f)$$

$$\mathbf{K}(X, t_{\text{in}}) = \mathbf{K}_{\text{in}}(X), \quad \text{in } \mathcal{B}, \quad (42g)$$

$$J_{\mathbf{K}} \varrho_{\nu} \dot{\omega} - \text{Div}(J_{\mathbf{K}} \varrho_{\nu} \mathbf{D} \text{Grad} \omega) = -J_{\mathbf{K}} \varrho_{\nu} r_{\text{n}} \omega - J_{\mathbf{K}} \varrho_{\nu} R_{\gamma(\text{ph})} \omega, \quad \text{in } \mathcal{B}, \quad (42h)$$

$$\omega = \omega_{\text{b}}, \quad \text{on } \partial_{\text{D}}^{\omega} \mathcal{B}, \quad (42i)$$

$$[-J_{\mathbf{K}} \varrho_{\nu} \mathbf{D} \text{Grad} \omega] \mathbf{N} = \mathcal{I}_{\text{b}}, \quad \text{on } \partial_{\text{N}}^{\omega} \mathcal{B}, \quad (42j)$$

$$\omega(X, t_{\text{in}}) = \omega_{\text{in}}(X), \quad \text{in } \mathcal{B}, \quad (42k)$$

531 where the operator $\text{dev}_{\mathbf{C}}$ is defined by $\text{dev}_{\mathbf{C}} \mathbf{T} := \mathbf{T} - \frac{1}{3} \text{tr}(\mathbf{C} \mathbf{T}) \mathbf{C}^{-1}$, for all second-order, contravari-
 532 ant tensors \mathbf{T} . Note that Equations (42d) and (42e) are obtained by left-multiplying Equation (34d)
 533 by \mathbf{C}^{-1} , employing Equation (40) for the constitutive representation of \mathbf{Y}_{u} , and extracting once
 534 the symmetric part and once the skew-symmetric part of the resulting expression. Moreover, we
 535 remark that Equation (42d) is equivalent to

$$J_{\mathbf{K}} \mathbf{b}_{\nu} \text{dev}\{\mathbf{C} \mathbf{K}^{-1} \dot{\mathbf{K}} \mathbf{C}^{-1} + (\mathbf{K}^{-1} \dot{\mathbf{K}})^{\text{T}}\} = -\text{dev} \mathbf{H} + \text{dev} \mathbf{Z}, \quad \text{in } \mathcal{B}. \quad (43)$$

536 Once the IBVP (42a)–(42k) is solved, the Lagrange multipliers $\mu_{\mathbf{K}}$ and $\mu_{\mathfrak{Z}}$ can be computed *a*
 537 *posteriori* as prescribed by Equations (33c) and (30b), respectively, i.e.,

$$\mu_{\mathbf{K}} = \frac{1}{3} \text{tr} \mathbf{Z} - \frac{1}{3} \text{tr} \mathbf{H} - \frac{1}{3} J_{\mathbf{K}} [\mathbf{a}_{\nu} + 2\mathbf{b}_{\nu}] \text{tr}(\mathbf{K}^{-1} \dot{\mathbf{K}}) = \frac{1}{3} \text{tr} \mathbf{Z} - \frac{1}{3} \text{tr} \mathbf{H} - \frac{1}{3} J_{\mathbf{K}} [\mathbf{a}_{\nu} + 2\mathbf{b}_{\nu}] R_{\gamma(\text{ph})}, \quad \text{in } \mathcal{B}, \quad (44a)$$

$$\mu_{\mathfrak{Z}} = -\mu_{\mathbf{K}} R_{\gamma(\text{ph})} = -\left\{ \frac{1}{3} \text{tr} \mathbf{Z} - \frac{1}{3} \text{tr} \mathbf{H} - \frac{1}{3} J_{\mathbf{K}} [\mathbf{a}_{\nu} + 2\mathbf{b}_{\nu}] R_{\gamma(\text{ph})} \right\} R_{\gamma(\text{ph})}, \quad \text{in } \mathcal{B}. \quad (44b)$$

538 Also the internal generalized force conjugated with \mathfrak{Z} , i.e., \mathcal{Y}_{u} , can be determined *a posteriori* by
 539 means of Equation (31), with $\mathcal{Z} = \mathbf{0}$, as

$$\mathcal{Y}_{\text{u}} = -\mu_{\mathfrak{Z}} = \mu_{\mathbf{K}} R_{\gamma(\text{ph})} = \left\{ \frac{1}{3} \text{tr} \mathbf{Z} - \frac{1}{3} \text{tr} \mathbf{H} - \frac{1}{3} J_{\mathbf{K}} [\mathbf{a}_{\nu} + 2\mathbf{b}_{\nu}] R_{\gamma(\text{ph})} \right\} R_{\gamma(\text{ph})}. \quad (45)$$

540 In our opinion, Equations (44a), (44b), and (45) deserve specific comments, which we summarize
 541 in Remarks 8.1 and 8.2 of section 8.

542 6.4 The limit case of spherical growth tensor

543 In several problems addressing the growth of a tumor in the so-called “*avasascular stage*” [25], the
 544 growth tensor is often assumed to be spherical from the outset [9, 11, 100, 59, 58]. By considering
 545 the decomposition $\mathbf{K} = J_{\mathbf{K}}^{1/3} \tilde{\mathbf{K}}$ (see e.g. [20] in which such decomposition is used for \mathbf{F} to

546 study incompressibility in finite deformations), which implies $\det \mathbf{K} = J_{\mathbf{K}}$ and, thus, necessarily
 547 $\det \tilde{\mathbf{K}} = 1$, the hypothesis of spherical growth tensor amounts to set $\tilde{\mathbf{K}} = \mathbf{I}$ and, thus, $\mathbf{K} = J_{\mathbf{K}}^{1/3} \mathbf{I}$.
 548 Consequently, \mathbf{K} features one free component only, i.e., $J_{\mathbf{K}}$, which, in turn, is restricted by Equation
 549 (3) to fulfill the constraint

$$\dot{J}_{\mathbf{K}} = R_{\gamma(\text{ph})} J_{\mathbf{K}}, \quad (46)$$

550 as can be seen by employing the identity $\text{tr}(\mathbf{K}^{-1} \dot{\mathbf{K}}) = \dot{J}_{\mathbf{K}}/J_{\mathbf{K}}$.

551 Since, in the present case, it holds true that $\mathbf{K}^{-1} \dot{\mathbf{K}} = \frac{1}{3}(\dot{J}_{\mathbf{K}}/J_{\mathbf{K}}) \mathbf{I}$, and, accordingly, $\mathbf{K}^{-1} \delta \mathbf{K} =$
 552 $\frac{1}{3}(\delta J_{\mathbf{K}}/J_{\mathbf{K}}) \mathbf{I}$, the non-spherical parts of the growth-conjugated, stress-like generalized forces \mathbf{Y}_{u} and
 553 \mathbf{Z} are filtered out from the PVW stated in Equations (27) and (28), so that Equation (29d), or,
 554 equivalently, Equation (32a), reduces to

$$(y_{\text{u}} + \mu_{\mathbf{K}}) - z = 0, \quad (47)$$

555 with $y_{\text{u}} := \frac{1}{3} \text{tr} \mathbf{Y}_{\text{u}}$ and $z := \frac{1}{3} \text{tr} \mathbf{Z}$ being the scalar coefficients of the spherical parts of \mathbf{Y}_{u} and \mathbf{Z} ,
 556 respectively (cf. Equation (33c)). Note that all the other equations of the boundary value problem
 557 (29a)–(29h) remain unchanged, and that Equation (29g), or its explicit form (32b), simply returns
 558 Equation (46). A direct consequence of these facts is that Equation (33a) is eliminated from the
 559 model and, consistently with what is usually done in some works (see e.g. [8, 11, 100, 99, 58] and
 560 the references therein), $J_{\mathbf{K}}$ is entirely defined by Equation (46), which, however, is here understood
 561 as a constraint. As such, it requires the Lagrange multiplier $\mu_{\mathbf{K}}$, which is computed by the force
 562 balance (47), i.e.,

$$\mu_{\mathbf{K}} = z - y_{\text{u}}, \quad (48)$$

563 similarly to Equation (33c). There remains to determine y_{u} . To do this, we go through the
 564 dissipation inequality, for example in the form of Equation (37), which we reformulate for the case
 565 at hand by assuming $\Psi_{\text{R}} = \hat{\Psi}_{\text{R}} \circ (\mathbf{F}, J_{\mathbf{K}})$. Hence, after some calculations, we obtain

$$y_{\text{u}} = y_{\text{u,d}} + J_{\mathbf{K}} \left[\frac{\partial \hat{\Psi}_{\text{R}}}{\partial J_{\mathbf{K}}} \circ (\mathbf{F}, J_{\mathbf{K}}) \right], \quad (49)$$

566 where the second summand on the right-hand-side of Equation (49) is the scalar coefficient of the
 567 spherical part of Eshelby stress tensor and $y_{\text{u,d}}$ is the dissipative part of y_{u} , and must comply with
 568 Equation (39), which now reads

$$\mathcal{D}_{\text{R}} = y_{\text{u,d}} (\dot{J}_{\mathbf{K}}/J_{\mathbf{K}}) \geq 0. \quad (50)$$

569 Within the linear theory, we can take $y_{\text{u,d}} = \kappa_{\nu} \dot{J}_{\mathbf{K}}$, with $\kappa_{\nu} > 0$, so that Equation (48) becomes

$$\mu_{\mathbf{K}} = z - J_{\mathbf{K}} \left[\frac{\partial \hat{\Psi}_{\text{R}}}{\partial J_{\mathbf{K}}} \circ (\mathbf{F}, J_{\mathbf{K}}) \right] - \kappa_{\nu} \dot{J}_{\mathbf{K}} = z - J_{\mathbf{K}} \left[\frac{\partial \hat{\Psi}_{\text{R}}}{\partial J_{\mathbf{K}}} \circ (\mathbf{F}, J_{\mathbf{K}}) \right] - J_{\mathbf{K}} \kappa_{\nu} R_{\gamma(\text{ph})}. \quad (51)$$

570 For completeness, we recall that \mathcal{Y}_{u} and $\mu_{\overline{\mathbf{T}}}$ are determined by adapting Equation (45) to the case
 571 under study. In conclusion, a theory of the type just described permits to compute χ and $J_{\mathbf{K}}$ by
 572 solving Equations (42a)–(42c) and (46), whereas the Lagrange multiplier $\mu_{\mathbf{K}}$ can be determined *a*
 573 *posteriori*, since it is decoupled from the rest of the model equations.

574 7 Comparison with Gurtin's derivation of Cahn-Hilliard equation

575 A rather different situation from that depicted in the previous section arises when the mass balance
 576 law accounts for diffusion. We consider this circumstance by adhering to the framework developed
 577 by Gurtin [74], in which the evolution of the mass density of a body is studied under the assumption
 578 that such mass density describes an order parameter⁷. We notice that, in the context of tumor
 579 growth, Cahn-Hilliard based models have been proposed, e.g., in [1, 2], whereas a model involving
 580 the curvature induced by the growth tensor was proposed in [36].

581 To model diffusion, we rewrite the mass balance law as $\dot{\varrho}_R = -\text{Div}\mathfrak{J}_R + Jr_\gamma$, where \mathfrak{J}_R is a
 582 diffusive mass flux vector, and the mass density ϱ_R is now regarded as a body's order parameter
 583 [74]. In fact, by using the relation $\varrho_R = J_{\mathbf{K}}\varrho_\nu$, and assuming ϱ_ν to be constant, one may regard
 584 $J_{\mathbf{K}}$ as the "effective" order parameter of the theory and rewrite the mass balance law as

$$\frac{\dot{J}_{\mathbf{K}}}{J_{\mathbf{K}}} = -\frac{1}{J_{\mathbf{K}}}\text{Div}\mathbf{v} + R_{\gamma(\text{ph})}, \quad (52)$$

585 with $\mathbf{v} := \varrho_\nu^{-1}\mathfrak{J}_R$ being a normalized mass flux vector having physical dimensions of velocity.

586 Equation (52) is the new form of the constraint on $J_{\mathbf{K}}$, and is a partial differential equation, in
 587 which \mathbf{v} has to be determined constitutively. To accomplish this task, we briefly review Gurtin's
 588 approach [74], and slightly modify it in order to match our growth problem. To start with, we recall
 589 that Gurtin's fundamental hypothesis is that the mass balance law described by Equation (52) has
 590 to be studied in conjunction with an additional balance of forces [74], dual to the variations of
 591 the order parameter. In this respect, the force balance in Equation (47) has to be re-interpreted
 592 accordingly, and, by introducing the virtual variations of the mass density ϱ_R and of $J_{\mathbf{K}}$, i.e., $\delta\varrho_R$
 593 and $\delta J_{\mathbf{K}}/J_{\mathbf{K}}$, we write it in the following two equivalent forms

$$-\text{Div}\boldsymbol{\xi} + \pi = \gamma, \quad \text{work-conjugate with } \delta\varrho_R \text{ (see [74])}, \quad (53a)$$

$$-\text{Div}\mathbf{f} + \left(\mathbf{f} \frac{\text{Grad}J_{\mathbf{K}}}{J_{\mathbf{K}}} + q_u + \mu_{\mathbf{K}} \right) = z, \quad \text{work-conjugate with } \frac{\delta J_{\mathbf{K}}}{J_{\mathbf{K}}}. \quad (53b)$$

594 Thus, a comparison of Equation (53b) with Equation (47) allows to identify the internal generalized
 595 force y_u with the combination

$$y_u \equiv -\text{Div}\mathbf{f} + \left(\mathbf{f} \frac{\text{Grad}J_{\mathbf{K}}}{J_{\mathbf{K}}} + q_u \right) = -\text{Div}\mathbf{f} + q_{u,\text{eff}}, \quad (54a)$$

$$q_{u,\text{eff}} := \mathbf{f} \frac{\text{Grad}J_{\mathbf{K}}}{J_{\mathbf{K}}} + q_u, \quad (54b)$$

596 where q_u is the generalized internal force associated with growth, while $q_{u,\text{eff}}$ describes an *effective*
 597 *internal force*, in which the term $\mathbf{f}J_{\mathbf{K}}^{-1}\text{Grad}J_{\mathbf{K}}$ accounts for the inhomogeneity of $J_{\mathbf{K}}$, and is indeed
 598 remnant of the "*inhomogeneity force*" introduced by Epstein and Maugin [41] in the context of
 599 growth mechanics (see also [101] for a more general context). We remark that Equations (53a) and
 600 (53b) can be found by adapting the PVW in Equation (27) to a theory of grade one in $J_{\mathbf{K}}$. This, in
 601 general, also requires prescribing $\mathbf{f}\mathbf{N}$ on the portions of $\partial\mathcal{B}$ on which contact forces dual to $\delta J_{\mathbf{K}}/J_{\mathbf{K}}$,
 602 or to $\delta\varrho_R$, are assigned. However, by assuming for simplicity no contact forces of this type, the

⁷The content of this section has been partially inspired by Fried and Sellers [50].

603 adapted expression of the PVW is obtained by adding the internal virtual work $\int_{\mathcal{B}}(\mathbf{f}/J_{\mathbf{K}})\text{Grad}\delta J_{\mathbf{K}}$ to
604 the left-hand side of Equation (27), replacing the second, fourth and sixth integrand on the same side
605 with $q_{\text{u}}\delta J_{\mathbf{K}}/J_{\mathbf{K}}$, $\mu_{\mathbf{K}}\{\delta J_{\mathbf{K}}/J_{\mathbf{K}} + [J_{\mathbf{K}}^{-1}\text{Div}\mathbf{v} - R_{\gamma(\text{ph})}]\delta\mathcal{T}\}$, and $\delta\mu_{\mathbf{K}}t_{\text{c}}\{\dot{J}_{\mathbf{K}}/J_{\mathbf{K}} + [J_{\mathbf{K}}^{-1}\text{Div}\mathbf{v} - R_{\gamma(\text{ph})}]\}$,
606 respectively, and substituting the third integrand on the right-hand side with $z\delta J_{\mathbf{K}}/J_{\mathbf{K}}$. This way,
607 the Lagrange multiplier $\mu_{\bar{\mathbf{x}}}$ is equal to the product of $\mu_{\mathbf{K}}$ with the negative of the right-hand side
608 of Equation (52).

609 Note that, up to the sign convention, we used Gurtin's notation in Equation (53a) for the
610 vectorial generalized force $\boldsymbol{\xi}$ as well as for the scalar-valued, internal generalized force π and external
611 generalized force γ [74]. Moreover, the forces \mathbf{f} , q_{u} , and z , which we introduced in Equation (53b)
612 for our problem, are connected with $\boldsymbol{\xi}$, π , and γ , respectively, through the conversion formulae

$$\mathbf{f} \equiv \varrho_{\text{R}}\boldsymbol{\xi}, \quad (55\text{a})$$

$$q_{\text{u}} + \mu_{\mathbf{K}} \equiv \varrho_{\text{R}}\pi, \quad (55\text{b})$$

$$z \equiv \varrho_{\text{R}}\gamma. \quad (55\text{c})$$

613 We emphasize that the Lagrange multiplier $\mu_{\mathbf{K}}$ does not feature explicitly in the derivation of
614 Equation (53a) done by Gurtin [74]. Rather, another multiplier, with different sign and different
615 physical dimensions, is introduced when the dissipation inequality is investigated. In fact, Gurtin's
616 Lagrange multiplier is a rescaled version of μ_{ch} featuring in Equation (35).

617 Before going further, we deem appropriate to recall that Gurtin [74] considered a body that
618 can be described as a “lattice”, or as a “network”, whose sites are free to experience relative
619 motions with respect to their underlying lattice structure [74]. A physical interpretation of $\boldsymbol{\xi}$, π ,
620 and γ , which are said to be “microforces” [74], is provided also by Podio Guidugli [109]. Here, by
621 slightly reformulating Gurtin and Podio Guidugli's words [74, 109], we say that $\boldsymbol{\xi}$ models contact
622 interactions that a given region $\mathcal{R} \subset \mathcal{B}$ of the body exchanges with the neighboring regions through
623 its boundary $\partial\mathcal{R}$, π describes the interactions exchanged between the lattice and the particles
624 occupying the lattice sites within \mathcal{R} (given that the particles and the lattice are subsystems of the
625 system realized by the complex made of particles and lattice, the force π is internal to the latter
626 system), while γ accounts for non-contact interactions between \mathcal{R} and its environment.

627 To motivate the employment of the above outlined framework for a problem of growth, and
628 especially of tumor growth, we remark that, as anticipated above, the external force denoted by γ
629 or z may represent, for instance, genetic or epigenetic interactions that are capable of modifying
630 the tumor mass through changes of its density ϱ_{R} , or, equivalently, of the descriptor $J_{\mathbf{K}}$, while the
631 complex consisting of lattice and particles (cf. [109]) may be taken as a representation of the system
632 comprising the cells (which play the role of the particles) and the network of collagen filaments (i.e.,
633 the “lattice”).

634 Next, we turn to the dissipation inequality. Hence, we modify Equation (35) to account for the
635 powers associated with the mass flux \mathbf{v} and the force \mathbf{f} , thereby obtaining

$$\int_{\mathcal{R}} \mathcal{D}_{\text{R,new}} = \int_{\mathcal{R}} \mathcal{D}_{\text{R,old}} + \int_{\partial\mathcal{R}} \mathbf{f}[\dot{J}_{\mathbf{K}}/J_{\mathbf{K}}]\mathbf{N} - \int_{\partial\mathcal{R}} \mu_{\text{ch}}J_{\mathbf{K}}^{-1}\mathbf{v}\mathbf{N} \geq 0, \quad (56)$$

636 where $\int_{\mathcal{R}} \mathcal{D}_{\text{R,old}}$ coincides with the right-hand-side of Equation (35) in which, however, the iden-
637 tification $\mathbf{Z} : \mathbf{K}^{-1}\dot{\mathbf{K}} = zJ_{\mathbf{K}}^{-1}\dot{J}_{\mathbf{K}}$ is made. By localizing this result, setting $\mu_{\text{ch}} = -\mu_{\mathbf{K}}$, and using
638 the force balance (53b) and the mass balance (52), we find

$$\mathcal{D}_{\text{R,new}} = -\dot{\Psi}_{\text{R}} + \mathbf{P} : \dot{\mathbf{F}} + q_{\text{u}}J_{\mathbf{K}}^{-1}\dot{J}_{\mathbf{K}} + \mathbf{f}J_{\mathbf{K}}^{-1}\text{Grad}\dot{J}_{\mathbf{K}} + \mathbf{v}\text{Grad}(J_{\mathbf{K}}^{-1}\mu_{\mathbf{K}}) \geq 0. \quad (57)$$

639 To complete the study of the dissipation inequality (57), we choose \mathbf{F} , $J_{\mathbf{K}}$, $\text{Grad}J_{\mathbf{K}}$, $\dot{J}_{\mathbf{K}}$, $J_{\mathbf{K}}^{-1}\mu_{\mathbf{K}}$,
640 and $\text{Grad}(J_{\mathbf{K}}^{-1}\mu_{\mathbf{K}})$ as independent variables, and we express $\Psi_{\mathbf{R}}$, \mathbf{P} , q_{u} , \mathbf{f} , and \mathbf{v} as functions of
641 these variables. Then, by following the Coleman-Noll procedure, and exploiting the fact that the
642 constitutive expressions of $\Psi_{\mathbf{R}}$, \mathbf{P} , and \mathbf{f} can be proven to be independent of $\dot{J}_{\mathbf{K}}$, $J_{\mathbf{K}}^{-1}\mu_{\mathbf{K}}$, and
643 $\text{Grad}(J_{\mathbf{K}}^{-1}\mu_{\mathbf{K}})$, we obtain

$$\mathbf{P} \equiv \hat{\mathbf{P}} \circ (\mathbf{F}, J_{\mathbf{K}}, \text{Grad}J_{\mathbf{K}}) := \frac{\partial \hat{\Psi}_{\mathbf{R}}}{\partial \mathbf{F}} \circ (\mathbf{F}, J_{\mathbf{K}}, \text{Grad}J_{\mathbf{K}}), \quad (58a)$$

$$q_{\text{u}} := q_{\text{u,d}} + J_{\mathbf{K}} \left[\frac{\partial \hat{\Psi}_{\mathbf{R}}}{\partial J_{\mathbf{K}}} \circ (\mathbf{F}, J_{\mathbf{K}}, \text{Grad}J_{\mathbf{K}}) \right], \quad (58b)$$

$$\mathbf{f} \equiv \hat{\mathbf{f}} \circ (\mathbf{F}, J_{\mathbf{K}}, \text{Grad}J_{\mathbf{K}}) := J_{\mathbf{K}} \left[\frac{\partial \hat{\Psi}_{\mathbf{R}}}{\partial \text{Grad}J_{\mathbf{K}}} \circ (\mathbf{F}, J_{\mathbf{K}}, \text{Grad}J_{\mathbf{K}}) \right], \quad (58c)$$

644 where $q_{\text{u,d}}$ is referred to as the dissipative part of q_{u} , in analogy with the definition of the force $y_{\text{u,d}}$
645 in Equation (49). Thus, we are left with the residual dissipation

$$\mathcal{D}_{\mathbf{R},\text{new}} = q_{\text{u,d}} J_{\mathbf{K}}^{-1} \dot{J}_{\mathbf{K}} + \mathbf{v} \text{Grad}(J_{\mathbf{K}}^{-1}\mu_{\mathbf{K}}) \geq 0, \quad (59)$$

646 which allows to take

$$q_{\text{u,d}} \equiv \hat{q}_{\text{u,d}} \circ (\mathbf{F}, J_{\mathbf{K}}, \text{Grad}J_{\mathbf{K}}, \dot{J}_{\mathbf{K}}, J_{\mathbf{K}}^{-1}\mu_{\mathbf{K}}, \text{Grad}(J_{\mathbf{K}}^{-1}\mu_{\mathbf{K}})) := \kappa_{\nu} \dot{J}_{\mathbf{K}}, \quad (60a)$$

$$\mathbf{v} \equiv \hat{\mathbf{v}} \circ (\mathbf{F}, J_{\mathbf{K}}, \text{Grad}J_{\mathbf{K}}, \dot{J}_{\mathbf{K}}, J_{\mathbf{K}}^{-1}\mu_{\mathbf{K}}, \text{Grad}(J_{\mathbf{K}}^{-1}\mu_{\mathbf{K}})) := \mathfrak{M} \text{Grad} \left(\frac{\mu_{\mathbf{K}}}{J_{\mathbf{K}}} \right), \quad (60b)$$

647 where $\kappa_{\nu} > 0$ can be understood as a strictly positive, bulk generalized viscosity, and the positive
648 semi-definite, second-order tensor field \mathfrak{M} is said to be the medium's *mobility tensor* [74].

649 Now, the growth law $R_{\gamma(\text{ph})}$ is prescribed phenomenologically, the normalized mass flux \mathbf{v} is
650 given by Equation (60b), and the Lagrange multiplier $\mu_{\mathbf{K}}$ can be expressed as a combination of
651 the other forces featuring in the force balance (53b), i.e.,

$$\mu_{\mathbf{K}} = z - q_{\text{u}} - \mathbf{f} \frac{\text{Grad}J_{\mathbf{K}}}{J_{\mathbf{K}}} + \text{Div}\mathbf{f} = z - \kappa_{\nu} \dot{J}_{\mathbf{K}} - J_{\mathbf{K}} \mathcal{E}_{J_{\mathbf{K}}}\Psi_{\mathbf{R}}, \quad (61)$$

652 where we introduced the notation

$$\mathcal{E}_{J_{\mathbf{K}}}\Psi_{\mathbf{R}} := \frac{\partial \hat{\Psi}_{\mathbf{R}}}{\partial J_{\mathbf{K}}} \circ (\mathbf{F}, J_{\mathbf{K}}, \text{Grad}J_{\mathbf{K}}) - \text{Div} \left[\frac{\partial \hat{\Psi}_{\mathbf{R}}}{\partial \text{Grad}J_{\mathbf{K}}} \circ (\mathbf{F}, J_{\mathbf{K}}, \text{Grad}J_{\mathbf{K}}) \right]. \quad (62)$$

653 Thus, we have enough information to determine $J_{\mathbf{K}}$ and $\mu_{\mathbf{K}}$, which, indeed, are obtained by solving
654 the system of equations

$$\frac{\dot{J}_{\mathbf{K}}}{J_{\mathbf{K}}} = -\frac{1}{J_{\mathbf{K}}} \text{Div} \left[\mathfrak{M} \text{Grad} \left(\frac{\mu_{\mathbf{K}}}{J_{\mathbf{K}}} \right) \right] + R_{\gamma(\text{ph})}, \quad (63a)$$

$$\frac{\mu_{\mathbf{K}}}{J_{\mathbf{K}}} = \frac{z}{J_{\mathbf{K}}} - \kappa_{\nu} \frac{\dot{J}_{\mathbf{K}}}{J_{\mathbf{K}}} - \mathcal{E}_{J_{\mathbf{K}}}\Psi_{\mathbf{R}}. \quad (63b)$$

655 8 Conclusions

656 In this work, we have proposed a formulation of the mechanics of bulk growth in which the rate
 657 of variation of the mass of a body is assigned from the outset through a growth law prescribed
 658 phenomenologically. To better capture the implications of our approach, we summarize our results
 659 as follows.

660 8.1 Main results within the theory of null grade in the growth tensor

661 In Section 3, and, in particular, by means of Equations (3), (4), (7), and (8), we have shown the
 662 phenomenological assignment of the growth law and the rephrasing of the mass balance law in light
 663 of the BKL decomposition, which allows to interpret the mass balance law itself as a non-holonomic
 664 and rheonomic constraint on the growth tensor. This constraint has then been put in Pfaffian form
 665 [95] in Equation (20a), thereby establishing the basis for introducing the virtual variations $\delta\mathbf{K}$, $\delta\mathcal{T}$,
 666 and $\delta\mathfrak{T}$, where \mathfrak{T} is the fictitious Lagrangian parameter representing time [106]. The main result of
 667 this formulation is given by Equations (19) and (20b), in which the constraint on the growth tensor
 668 is expressed in terms of the generalized virtual displacements $\delta\mathbf{K}$, $\delta\mathcal{T}$, and $\delta\mathfrak{T}$, and is attached to
 669 the “constrained version” of the PVW. This version of the PVW constitutes the crux of our work,
 670 and is presented in detail in Section 5, where we revise the PVW, and obtain the boundary value
 671 problem (34a)–(34e) of interest for the study at hand.

672 In Section “Constitutive laws and final form of the initial and boundary value problem”, after
 673 presenting the constitutive framework, studying the dissipation inequality, and showing the final
 674 form of the initial and boundary value problem in Equations (42a)–(42k), we obtain the first results
 675 concerning the generalized internal forces \mathcal{Y}_u and $\mathbf{Y}_{u,d}$ as well as the Lagrange multipliers $\mu_{\mathfrak{T}}$ and
 676 $\mu_{\mathbf{K}}$. These results serve as comments to Equations (44a), (44b), and (45), and can be summarized
 677 in the following remarks:

678 **Remark 8.1 (The case of no mass variation, i.e., $R_{\gamma(\text{ph})} = 0$)**

679 *If we set $R_{\gamma(\text{ph})} = 0$, thereby switching off the variation of mass, we find $\mathcal{Y}_u = -\mu_{\mathfrak{T}} = 0$. This
 680 result, which trivially follows from Equation (45), is consistent with the fact that, for $R_{\gamma(\text{ph})} = 0$, the
 681 constraint (7) becomes holonomic, and amounts to requiring that the growth-induced distortions are
 682 isochoric, i.e., $\dot{\mathbf{J}}_{\mathbf{K}} = 0$ (see also Equation (34e)). In this case, the fictitious Lagrangian parameter
 683 \mathfrak{T} need not be introduced at all, and, accordingly, Equations (29e) and (30a) disappear from the
 684 model, while the Lagrange multiplier $\mu_{\mathbf{K}}$ reduces to $\mu_{\mathbf{K}} = \frac{1}{3}\text{tr}\mathbf{Z} - \frac{1}{3}\text{tr}\mathbf{H}$, with $-\frac{1}{3}\text{tr}\mathbf{H}$ acquiring
 685 the meaning of a generalized, “configurational” pressure [64], and \mathbf{H} being evaluated for admissible
 686 tensors \mathbf{K} . On the other hand, the evolution of $\mathbf{K}^{-1}\dot{\mathbf{K}}$, which is a deviatoric tensor, is governed by
 687 Equation (34d). Thus, in general, even for vanishing $\text{dev}\mathbf{Z}$, the configurational force $-\text{dev}\mathbf{H}$ may
 688 trigger the evolution of non-trivial, plastic-like distortions, described by the isochoric tensor field
 689 \mathbf{K} , as shown in Equation (42d). In this respect, some linear models of the biomechanical process
 690 known as “remodeling” are recovered [7, 64, 105, 68]. Finally, we notice that, since it holds true
 691 that $\text{tr}\mathbf{Y}_{u,d} = J_{\mathbf{K}}[\mathbf{a}_\nu + 2\mathbf{b}_\nu]\text{tr}(\mathbf{K}^{-1}\dot{\mathbf{K}})$ and $\text{tr}(\mathbf{K}^{-1}\dot{\mathbf{K}}) = R_{\gamma(\text{ph})}$, the vanishing of $R_{\gamma(\text{ph})}$ also implies
 692 the vanishing of the volumetric part of the dissipative generalized force $\mathbf{Y}_{u,d}$. Still, the converse is
 693 not true, as highlighted by Remark 8.2.*

694 **Remark 8.2 (The case of vanishing $\text{tr}\mathbf{Y}_{u,d}$)**

695 *Since it descends from Equation (40) that $\text{tr}\mathbf{Y}_{u,d} = J_{\mathbf{K}}[\mathbf{a}_\nu + 2\mathbf{b}_\nu]\text{tr}(\mathbf{K}^{-1}\dot{\mathbf{K}})$, one may consider the*

696 case $\mathbf{a}_\nu + 2\mathbf{b}_\nu = 0$, thereby characterizing the situation in which the spherical component of the
697 dissipative generalized force $\mathbf{Y}_{\mathbf{u},d}$ vanishes identically, regardless of the values taken by $\text{tr}(\mathbf{K}^{-1}\dot{\mathbf{K}})$.
698 Also in this situation, the Lagrange multiplier $\mu_{\mathbf{K}}$ reduces to the configurational pressure $\mu_{\mathbf{K}} =$
699 $\frac{1}{3}\text{tr}\mathbf{Z} - \frac{1}{3}\text{tr}\mathbf{H}$, but, as long as the condition $R_{\gamma(\text{ph})} \neq 0$ is fulfilled, growth persists and the evolution
700 of \mathbf{K} is fully determined by Equations (34d) and (34e). Growth, thus, continues to be a dissipative
701 process.

702 In Section 6.4, we showed how our approach can be used to recover systematically the situation,
703 often encountered in the modeling of tumor growth, in which the growth tensor is assumed to be
704 spherical from the outset [8, 11, 59, 56]. Also for this situation, which can be described in terms of
705 the determinant of the growth tensor, i.e., $J_{\mathbf{K}}$, we discussed separately the limit cases of no growth
706 (cf. Remark 8.1) and of vanishing dissipative force $y_{\mathbf{u},d}$ (cf. Remark 8.2). These can be summarized
707 as follows:

- 708 • The case of no growth (see Remark 8.1) trivially restricts $J_{\mathbf{K}}$ to remain equal to its initial
709 distribution, $J_{\mathbf{K}}^{\text{in}}$, while $\mu_{\mathbf{K}}$ becomes $\mu_{\mathbf{K}} = z - J_{\mathbf{K}}^{\text{in}}[\partial_{J_{\mathbf{K}}}\hat{\Psi}_{\text{R}} \circ (\mathbf{F}, J_{\mathbf{K}}^{\text{in}})]$, with z being possibly
710 null. The quantity $J_{\mathbf{K}}^{\text{in}}$, in fact, need not be unitary, in general, because the “initial” state
711 of the body may coincide with a state in which growth has occurred and has then come to a
712 stop (see e.g. [36]). Clearly, also in this case, no growth implies the vanishing of $y_{\mathbf{u},d}$, whereas
713 the vice versa, in general, does not apply.
- 714 • The discussion done in Remark 8.2 on the vanishing of $y_{\mathbf{u},d}$ is recovered for $\kappa_\nu = 0$, thereby
715 yielding $y_{\mathbf{u}} = J_{\mathbf{K}}[\partial_{J_{\mathbf{K}}}\hat{\Psi}_{\text{R}} \circ (\mathbf{F}, J_{\mathbf{K}})]$, and $\mu_{\mathbf{K}} = z - J_{\mathbf{K}}[\partial_{J_{\mathbf{K}}}\hat{\Psi}_{\text{R}} \circ (\mathbf{F}, J_{\mathbf{K}})]$, while the evolution
716 of $J_{\mathbf{K}}$ remains prescribed by Equation (46).

717 8.2 Main results within the Cahn-Hilliard theory

718 A result that we deem particularly relevant for our formulation is the reframing of the Cahn-
719 Hilliard model provided by Gurtin [74] within the context of the mechanics of bulk growth. This
720 has been discussed in Section 7. In particular, we remark that Equations (63a) and (63b), which
721 are obtained by adapting Gurtin’s procedure [74] to our problem, boil down to Equations (46) and
722 (51), respectively, if the body’s mobility tensor \mathfrak{M} is assumed to be null and if the dependence on
723 the strain energy density $\hat{\Psi}_{\text{R}}$ on $\text{Grad}J_{\mathbf{K}}$ is suppressed. Furthermore, we think that, in order to
724 highlight how our work is connected with that of others through a strongly similar physics, it could
725 be interesting to evaluate again the case of vanishing growth and the case of vanishing dissipative
726 force $q_{\mathbf{u},d}$ within the framework of the Cahn-Hilliard model. This can be summarized as follows:

727 **Remark 8.3 (Vanishing $R_{\gamma(\text{ph})}$ and vanishing $q_{\mathbf{u},d}$ within the Cahn-Hilliard approach)**
728 Equations (63a) and (63b) show that, quite differently from what has been said in Remark 8.1, the
729 condition $R_{\gamma(\text{ph})} = 0$ does not imply, in this case, $\dot{J}_{\mathbf{K}} = 0$. Rather, it prescribes that $J_{\mathbf{K}}$ evolves
730 according to the Cahn-Hilliard equation (63a), with $R_{\gamma(\text{ph})} = 0$, and that the Lagrange multiplier
731 $\mu_{\mathbf{K}}$ is determined by Equation (63b), possibly augmented with the supplementary condition $z = 0$,
732 if required. Thus, even in the absence of “true” growth, the movement of mass within the body,
733 described by the re-distribution of $J_{\mathbf{K}}$, is driven by diffusion. This result, in fact, recalls what
734 has been obtained by Epstein [40] in a work in which he hypothesized a sort of diffusion
735 equation for a tensor-valued field representing the “material inhomogeneities” of a body [101] (see

736 also [36] for the case in which Epstein’s framework was extended to biphasic media for studying
737 tumor growth). Indeed, within this scenario, a theory of growth based on the assumption of purely
738 volumetric growth tensor $\mathbf{K} = J_{\mathbf{K}}^{1/3} \mathbf{I}$ boils down to a Cahn-Hilliard model of diffusion for $J_{\mathbf{K}}$, with
739 the dissipative term $-\kappa_{\nu} \dot{J}_{\mathbf{K}}$, i.e.,

$$\dot{J}_{\mathbf{K}} = -\text{Div} \left[\mathfrak{M} \text{Grad} \left(\frac{\mu_{\mathbf{K}}}{J_{\mathbf{K}}} \right) \right], \quad (64a)$$

$$\frac{\mu_{\mathbf{K}}}{J_{\mathbf{K}}} = -\kappa_{\nu} \frac{\dot{J}_{\mathbf{K}}}{J_{\mathbf{K}}} - \mathcal{E}_{J_{\mathbf{K}}} \Psi_{\text{R}}. \quad (64b)$$

740 There is, however, another nuance concealed in the Cahn-Hilliard approach. Indeed, whereas in
741 the model discussed in Section “The limit case of spherical growth tensor” the case of no growth
742 ($R_{\gamma(\text{ph})} = 0$) also yields the vanishing of $q_{\text{u,d}}$, because it implies $\dot{J}_{\mathbf{K}} = 0$, this implication does not
743 hold true in the present framework, since the condition $R_{\gamma(\text{ph})} = 0$ does not require $\dot{J}_{\mathbf{K}} = 0$, and,
744 thus, it does not lead to $q_{\text{u,d}} = 0$. In fact, one can compell $q_{\text{u,d}}$ to be null by choosing $\kappa_{\nu} = 0$,
745 thereby re-obtaining the standard version of the Cahn-Hilliard model.

746 8.3 Connections with other theories of growth

747 The formulation of the mechanics of bulk growth proposed in this work may be regarded as a
748 “bridge” between the perspective supplied by Epstein and Maugin [41] and the ones developed by
749 DiCarlo and Quiligotti [38] and, later, by DiCarlo [37]. To explain this, let us briefly recall the
750 most important results of these two approaches.

751 8.3.1 Growth viewed as a “flow rule”.

752 Epstein and Maugin [41] write the mass balance law in a way similar to our Equation (3)⁸, but,
753 in their case, the source/sink of mass *is not* given phenomenologically. Rather, after showing how
754 to determine what they call “*transplant operator*” [41], i.e., *formally* the inverse of the growth
755 tensor used in our work, Epstein and Maugin [41] compute the source/sink of mass *a posteriori* as
756 $R_{\gamma} = \text{tr}(\mathbf{K}^{-1} \dot{\mathbf{K}})$ (in our notation). For a comparison, the Reader is referred to Equation (9.21) of
757 [41], in which our R_{γ} is written as “ Π/ρ_0 ”, and our $\text{tr}(\mathbf{K}^{-1} \dot{\mathbf{K}})$ replaces their “ $-\text{tr} \mathbf{L}_{\mathbf{K}}$ ”. To show
758 how to obtain \mathbf{K} , Epstein and Maugin [41] determine an evolution law for it, in which a suitable
759 rate of \mathbf{K} is expressed as a function of its power-conjugated generalized force, i.e., Eshelby stress
760 tensor. This result, in a sense, may be understood as a flow rule for a viscoplastic medium, as
761 recognized by DiCarlo [37], although its range of validity within a growth theory may need further
762 investigations. Indeed, in our opinion, one ought to make sure that $\text{tr}(\mathbf{K}^{-1} \dot{\mathbf{K}})$ does not vanish
763 identically for vanishing Eshelby stress, since this would imply that stress is the only activator, or
764 deactivator, of growth.

765 8.3.2 The “Eshelbian coupling” pointed out by DiCarlo and Quiligotti [38].

766 As anticipated in the Introduction, DiCarlo and Quiligotti [38] formulate a model of growth whose
767 core is the balance of the stress-like forces dual to the virtual variations of \mathbf{K} . In fact, this

⁸In fact, this is true up to the presence of a mass flux vector, which we neglect in the first part of our work and consider only afterwards, when we compare our approach with the one by Gurtin [74].

768 force balance is obtained without any *a priori* constraint on the growth tensor or its rate, and,
769 after establishing the constitutive framework and studying the system’s dissipation inequality, it is
770 written as $\mathbf{Y}_d + \mathbf{H} = \mathbf{Z}$ (in our notation), where \mathbf{Y}_d is the dissipative part of the overall generalized
771 internal force \mathbf{Y} (compare with our Equation (29d)). This way, DiCarlo and Quiligotti [38] highlight
772 the interaction between Eshelby stress tensor \mathbf{H} and the stress-like generalized force \mathbf{Y} (“ $-\mathbb{C}$ ” in
773 their notation). This interaction, referred to as “*Eshelbian coupling*” by DiCarlo and Quiligotti
774 [38], is mentioned also by DiCarlo [37] in conjunction with the role attributed to the generalized
775 force \mathbf{Z} (“ \mathbb{B} ” in his notation). Indeed, by rephrasing DiCarlo’s words [37], one may say that \mathbf{Z}
776 resolves the biochemical interactions that, possibly occurring at different scales, promote or hinder
777 the growth of a biological system, and models their influence on the mechanics of the system’s
778 structural evolution at the continuum scale. Thus, if we correctly interpret DiCarlo’s thoughts
779 [37], it is hard to construct a biologically consistent mechanical theory of growth without \mathbf{Z} , since
780 Eshelby stress tensor alone is unable to capture the necessary biological information that guides
781 growth. This, in turn, contrasts with the model of growth provided by Epstein and Maugin [41].

782 Even though we agree on the fact that the picture proposed by Epstein and Maugin [41] may be
783 too restrictive in “real” biological situations, since we believe that it is the force unbalance $\mathbf{Z} - \mathbf{H}$,
784 rather than \mathbf{H} , that should be considered in biological growth, our interpretation of the role of
785 Eshelby stress tensor is different from that given by DiCarlo and Quiligotti [38]. Indeed, in our
786 opinion, \mathbf{H} is the “*driving force*” [41] of the contribution to the overall variation of mass of a body
787 that is ascribable to the development and redistribution of “*material inhomogeneities*” [41, 101].
788 On the other hand, we think that also $\mathbf{Z} - \mathbf{H}$ may fail to describe some growth laws supported by
789 experiments. It is exactly this observation that suggested us to reformulate growth as a constrained
790 problem. This way, indeed, one is free to assign from the outset the growth law that best fits a
791 given phenomenology by just paying the price of introducing the Lagrange multiplier $\mu_{\mathbf{K}}$. In this
792 respect, this part of our approach seems to comply with the biochemical interactions discussed
793 in [37]. Furthermore, the Lagrange multiplier, although being by definition the dual force of the
794 variation of mass, need not feature explicitly in the mass balance, i.e., the constraint of the theory,
795 unless one resorts, for instance, to diffusion models, like the Cahn-Hilliard one discussed by Gurtin
796 [74], in which, besides R_γ (in our notation), the transport of mass is considered and associated with
797 the gradient of $\mu_{\mathbf{K}}$. In addition, in our approach (here limited to the case of isotropic material),
798 the deviatoric tensor $\text{dev}\mathbf{Z} - \text{dev}\mathbf{H}$ is the “*driving force*”, as predicted by Epstein and Maugin
799 [41], of the isochoric distortions associated with growth, but not directly related to the variation of
800 mass. These distortions, indeed, make the growth tensor generally non-spherical, thereby allowing
801 for models even more general than those usually encountered in the description of tumor growth. In
802 this respect, we have in mind also those growth models formulated for bone, skin, arteries or heart
803 mechanics, in which the growth tensor is assumed to be symmetric, but non-spherical, and with
804 principal (anisotropy) directions assigned from the outset (see [6, 5] for a review). According to our
805 model, instead, also in all these cases, \mathbf{K} has to be computed by solving Equations (42a)–(42k),
806 and it is a suitably modeled external force \mathbf{Z} that determines, through its interaction with Eshelby
807 stress tensor, i.e., through $\text{dev}\mathbf{Z} - \text{dev}\mathbf{H}$, how much \mathbf{K} deviates from a spherical tensor and which
808 symmetries it may possess (cf. Equation (42d)).

809 **8.3.3 Towards a unified approach to inelastic processes.**

810 As a final remark, let us notice that, since our approach is based on a growth law given *a priori*,
811 the variation of mass considered in our work need not be correlated, in principle, with any measure
812 of stress, although we do let $R_{\gamma(\text{ph})}$ depend on \wp , as reported in Equation (4). This fact emphasizes
813 that the constrained approach, although being constrained, guarantees a certain freedom in the
814 choice of the growth law; a freedom that is balanced by the restrictions placed on tensor \mathbf{K} . In
815 this respect, however, we think that our approach may be used also in physical situations deeply
816 different from growth, in which it is anyway necessary, or preferable, to assign the evolution of
817 \mathbf{K} *a priori*. Indeed, as an outlook for future research, we have in mind to reformulate in the
818 context of growth and/or remodeling some models of the inelastic phenomena taken from the
819 literature, like, for instance, Gurtin’s constrained plasticity [71, 72, 73], or the plastic flow rules
820 suggested by Mićunović [102], and obtained experimentally for the case of non-associative plasticity.
821 Furthermore, a natural extension of a theory of growth of grade one in the inelastic variable \mathbf{K}
822 would consist in switching to constitutive relations of grade two in the deformation. Although such
823 approaches, in fact, have been proposed for the case of bone remodeling by adopting linear energy
824 densities (see e.g. [54]), the framework of growth might call for the generalization of these energies
825 to the nonlinear case.

826 **Conflict of Interests**

827 The Authors declare that they have no conflict of interests.

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841 *From mechanobiology to smart devices.*”

842 **A1: Time as a fictitious, additional Lagrangian parameter**

843 To explain the reasons for regarding time as a fictitious, additional Lagrangian parameter of the
844 problem under investigation, let us briefly review the approach of Analytical Mechanics to a generic
845 discrete mechanical system [17] subjected to non-holonomic and rheonomic constraints [87]. To this

846 end, let us consider a system of this type, described by $n \geq 1$, $n \in \mathbb{N}$, free generalized coordinates,
 847 which, as is customary in Analytical Mechanics, are denoted by q^1, \dots, q^n . For each $k = 1, \dots, n$,
 848 let $q^k : [t_{\text{in}}, t_{\text{fin}}] \rightarrow \mathbb{R}$ be a function of time fulfilling all the differentiability hypotheses that are
 849 necessary for the forthcoming discussion. Let us also consider $m \in \mathbb{N}$, $m \leq n$, linearly independent,
 850 non-holonomic and rheonomic constraints, i.e., restrictions on the generalized velocities $\dot{q}^1, \dots, \dot{q}^n$
 851 that, under the hypotheses of linearity in $\dot{q}^1, \dots, \dot{q}^n$, can be expressed as

$$\tilde{\mathcal{C}}^i(q(t), \dot{q}(t), t) := \sum_{k=1}^n [a^i_k(q(t), t)] \dot{q}^k(t) + b^i(q(t), t) = 0, \quad i = 1, \dots, m, \quad (65)$$

852 where q denotes the array $q := (q^1, \dots, q^n)$, while the coefficients $a^i_k(q(t), t)$ and $b^i(q(t), t)$ are
 853 given functions of the generalized coordinates and time. We remark that the constraints defined in
 854 Equation (65) are analogous, for discrete systems, to those introduced in Equations (7) and (8).

855 Since the matrix constructed with the functions $a^i_k(q(t), t)$ has maximal rank for all t and
 856 $q(t)$, only $n - m$ generalized velocities can be taken as linearly independent in Equation (65).
 857 Accordingly, if the constraints are employed explicitly to select *a priori* the admissible motions of
 858 the system, the remaining m generalized velocities are to be understood as functions of the linearly
 859 independent ones as well as of the coefficients $b^i(q(t), t)$ and $a^i_k(q(t), t)$. The relations obtained this
 860 way must be respected also by the virtual velocities of the considered mechanical system, since, by
 861 definition, they must be instantaneously in harmony with the imposed constraints. In this respect,
 862 it can be noticed that, even when the linearly independent velocities are assumed to vanish, the
 863 coefficients $b^i(q(t), t)$, when they are nonzero, render the m dependent velocities (be they virtual
 864 or real) nonzero, too.

865 On the other hand, if the constraints (65) are accounted for through the method of Lagrange
 866 multipliers, framed within the context of the Principle of Virtual Work, the coefficients $b^i(q(t), t)$
 867 necessitate a dedicated study. Indeed, since they are not multiplied by any virtual displacement,
 868 they spoil the standard procedure on which the Principle of Virtual Work is based. To see this, let us
 869 define the virtual displacements $\delta q^1, \dots, \delta q^n$, and let us recall that, at each fixed time $t \in [t_{\text{in}}, t_{\text{fin}}]$,
 870 and for each $k = 1, \dots, n$, the symbol $\delta q^k(t)$ represents a virtual variation of the value taken by q^k
 871 at time t , i.e., $q^k(t)$. Hence, the collection $\delta q(t) := (\delta q^1(t), \dots, \delta q^n(t))$ represents a virtual variation
 872 of the system's global configuration at time t , i.e., $q(t)$, and the corresponding virtual work can be
 873 written as $\sum_{k=1}^n \mathcal{Q}_k(t) \delta q^k(t)$, where $\mathcal{Q}_k(t)$ denotes the Lagrange generalized force dual to $\delta q^k(t)$ ⁹.

874 Granted this background, as suggested by Lanczos [87], the constraints (65) can be reformulated
 875 as

$$\hat{\mathcal{C}}^i(q(t), \delta q(t), \delta t(t), t) = \sum_{k=1}^n [a^i_k(q(t), t)] \delta q^k(t) + b^i(q(t), t) \delta t(t) = 0, \quad i = 1, \dots, m, \quad (66)$$

876 where $\delta t(t)$ (“ δt ”, in Lanczos' original notation [87]) is a translation of time attached at the instant
 877 of time t .

878 By introducing m unknown, time-dependent Lagrange multipliers μ_1, \dots, μ_m , the quantity
 879 $\sum_{i=1}^m \sum_{k=1}^n \mu_i(t) \hat{\mathcal{C}}^i(q(t), \delta q(t), \delta t(t), t)$ produces the term $\sum_{i=1}^m \mu_i(t) [b^i(q(t), t)] \delta t(t)$, which, how-
 880 ever, cannot be combined with any of the summands of the virtual work $\sum_{k=1}^n \mathcal{Q}_k(t) \delta q^k(t)$, since

⁹It is out of the scopes of this discussion to provide a thorough analysis of the constitutive expressions of Lagrange generalized forces.

881 none of those features the variation $\delta t(t)$. To solve this problem, we proceed in two steps. First,
 882 we introduce the fictitious Lagrangian parameter $\mathfrak{T} : \mathcal{I} \rightarrow \mathcal{I}$, such that $\mathfrak{T}(t) = t_0 + t$, where
 883 $t_0 \in \mathcal{I}$ is a given constant. We say that the map \mathfrak{T} is a ‘‘fictitious Lagrangian parameter’’ because
 884 its evolution is already prescribed and is consistent with the transformation of time of Galileian
 885 mechanics, thereby yielding the condition $\dot{\mathfrak{T}}(t) = 1$, for all $t \in \mathcal{I}$. This condition, in fact, can be
 886 regarded as an additional constraint, and is satisfied as $\delta\mathfrak{T}(t) = \delta t(t)$, when it is written in terms
 887 of the virtual variation of \mathfrak{T} at t , denoted by $\delta\mathfrak{T}(t)$.

888 The second step consists of giving room to a generalized force dual to $\delta\mathfrak{T}(t)$ [106], hereafter called
 889 $\mathcal{Q}_{\mathfrak{T}}(t)$, so that the Principle of Virtual Work, augmented by the method of Lagrange multipliers,
 890 and accounting for all the constraints, yields

$$\begin{aligned} & \sum_{k=1}^n \mathcal{Q}_k(t) \delta q^k(t) + \mathcal{Q}_{\mathfrak{T}}(t) \delta\mathfrak{T}(t) \\ & + \sum_{i=1}^m \mu_i(t) \left\{ \sum_{k=1}^n [a^i_k(q(t), t)] \delta q^k(t) + b^i(q(t), t) \delta t(t) \right\} + \mu_{\mathfrak{T}}(t) \left\{ \delta\mathfrak{T}(t) - \delta t(t) \right\} = 0, \end{aligned} \quad (67)$$

891 where $\mu_{\mathfrak{T}}(t)$ is the Lagrange multiplier associated with the constraint $\delta\mathfrak{T}(t) - \delta t(t) = 0$. Hence,
 892 by putting together all the terms multiplied by the same virtual variation, Equation (67) can be
 893 rewritten as

$$\begin{aligned} & \sum_{k=1}^n \left\{ \mathcal{Q}_k(t) + \sum_{i=1}^m \mu_i(t) [a^i_k(q(t), t)] \right\} \delta q^k(t) \\ & + \left\{ \mathcal{Q}_{\mathfrak{T}}(t) + \mu_{\mathfrak{T}}(t) \right\} \delta\mathfrak{T}(t) + \left\{ \sum_{i=1}^m \mu_i(t) [b^i(q(t), t)] - \mu_{\mathfrak{T}}(t) \right\} \delta t(t) = 0, \end{aligned} \quad (68)$$

894 and leads to the system of equations

$$\mathcal{Q}_k(t) + \sum_{i=1}^m \mu_i [a^i_k(q(t), t)] = 0, \quad k = 1, \dots, n, \quad (69a)$$

$$\mathcal{Q}_{\mathfrak{T}}(t) + \mu_{\mathfrak{T}}(t) = 0, \quad \mathcal{Q}_{\mathfrak{T}}(t) = -\mu_{\mathfrak{T}}(t), \quad (69b)$$

$$\sum_{i=1}^m \mu_i(t) [b^i(q(t), t)] - \mu_{\mathfrak{T}}(t) = 0, \quad \mu_{\mathfrak{T}}(t) = \sum_{i=1}^m \mu_i(t) [b^i(q(t), t)], \quad (69c)$$

895 which, in conjunction with Equation (65), allow to determine the n Lagrangian parameters q^1, \dots, q^n ,
 896 the m Lagrange multipliers μ_1, \dots, μ_m , as well as $\mu_{\mathfrak{T}}$ and $\mathcal{Q}_{\mathfrak{T}}$. Note that, for brevity, in equations
 897 (67) and (68), we have omitted the terms $\sum_{i=1}^m \delta\mu_i(t) t_c \check{\mathcal{C}}^i(q(t), \dot{q}(t), t)$ and $\delta\mu_{\mathfrak{T}} t_c [\dot{\mathfrak{T}}(t) - 1]$, with
 898 $t_c > 0$ being a characteristic time. These terms, however, are identically zero.

899 **A2: The case of non-vanishing external time-conjugated force**

900 In this section, we sketch the main changes that take place in the procedure shown in section 6, if
 901 the hypothesis concerning the vanishing of \mathcal{Z} is relaxed and, rather, \mathcal{Z} is regarded as an unknown

902 of the problem. In this case, following Gurtin's approach [74], we postulate that the dissipation
 903 inequality reads

$$\int_{\mathcal{R}} \mathcal{D}_R = \int_{\mathcal{R}} \mathcal{D}_{R,\text{old}} + \int_{\mathcal{R}} \mathcal{Z} \dot{\mathfrak{T}} - \int_{\mathcal{R}} \mu_{\mathfrak{T}} \dot{\mathcal{T}} \geq 0, \quad (70)$$

904 where $\int_{\mathcal{R}} \mathcal{D}_{R,\text{old}}$ coincides with the right-hand side of Equation (35), with $\mu_{\text{ch}} \equiv -\mu_{\mathbf{K}}$, the term $\mathcal{Z} \dot{\mathfrak{T}}$
 905 is the external power done by \mathcal{Z} on $\dot{\mathfrak{T}}$, and the term $-\mu_{\mathfrak{T}} \dot{\mathcal{T}}$ is introduced in analogy with the last
 906 summand on the right-hand side of Equation (35) to account for the fact that $\dot{\mathfrak{T}}$ is constrained to
 907 be equal to $\dot{\mathcal{T}}$ from the outset, thereby allowing to identify $\dot{\mathcal{T}}$ as a "source" for $\dot{\mathfrak{T}}$. By performing
 908 the same localization procedure that has led to Equation (37) from Equation (35), recalling the
 909 force balance $\mathcal{Y}_u + \mu_{\mathfrak{T}} = \mathcal{Z}$ of Equation (29e), and enforcing the constraint $\dot{\mathfrak{T}} = \dot{\mathcal{T}}$, we obtain now

$$\mathcal{D}_R = -\dot{\Psi}_R + \mathbf{P} : \dot{\mathbf{F}} + \mathbf{Y}_u : \mathbf{K}^{-1} \dot{\mathbf{K}} + \mathcal{Y}_u \dot{\mathfrak{T}} \geq 0. \quad (71)$$

910 Thus, under the constitutive hypotheses presented in section 6.1, which declare $\hat{\Psi}_R$ as independent
 911 of \mathfrak{T} , and by assuming that $\mathcal{Y}_u \dot{\mathfrak{T}} = \mathcal{Y}_u \dot{\mathcal{T}} = \mathcal{Y}_u$ is not dissipative (recall that the last equality descends
 912 from the identity $\dot{\mathcal{T}}(X, t) = 1$), we conclude that the condition $\mathcal{Y}_u = 0$ must hold, and, thus, that
 913 Equation (71) yields Equation (39), i.e., $\mathcal{D}_R = \mathbf{Y}_{u,d} : \mathbf{K}^{-1} \dot{\mathbf{K}} \geq 0$. Hence, the study of the residual
 914 dissipation inequality, the solution of the IBVP (42a)–(42k), and the *a posteriori* determination of
 915 $\mu_{\mathbf{K}}$ and $\mu_{\mathfrak{T}}$ as shown in Equations (44a) and (44b) can proceed as shown in the main body of our
 916 work. However, the difference with respect to the model presented above is that Equation (29e)
 917 now determines \mathcal{Z} , because \mathcal{Y}_u vanishes for constitutive reasons, so that Equations (31) and (45)
 918 now become

$$\mathcal{Z} = \mu_{\mathfrak{T}} = -\mu_{\mathbf{K}} [\hat{R}_{\gamma(\text{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)] = -\left\{ \frac{1}{3} \text{tr} \mathbf{Z} - \frac{1}{3} \text{tr} \mathbf{H} - \frac{1}{3} J_{\mathbf{K}} [\mathbf{a}_\nu + 2\mathbf{b}_\nu] R_{\gamma(\text{ph})} \right\} R_{\gamma(\text{ph})}. \quad (72)$$

919 Therefore, also the conclusion reported in Remark 8.1 must be rephrased accordingly, by saying
 920 that, for $R_{\gamma(\text{ph})} = 0$, the condition $\mathcal{Z} = \mu_{\mathfrak{T}} = 0$ complies with the fact that the constraint (7) turns
 921 into a holonomic constraint.

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