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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-) 2 decomposition of the deformation gradient tensor, we study some peculiar mechanical aspects 3 of growth in a monophasic continuum by regarding the reformulated mass balance equation as 4 a non-holonomic and rheonomic constraint. Such constraint restricts the admissible rates of the 5 growth tensor, i.e., one of the two factors of the BKL-decomposition, to comply with a growth 6 law provided phenomenologically. For our purposes, we put the constraint in Pfaffian form, and 7 8 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 9 existence of generalized forces conjugated with the virtual variations of the growth tensor, and 10 we write a constrained version of the Principle of Virtual Work (PVW) that leads to a mixed 11 12 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 13 role that the growth-conjugated forces play on the components of the growth tensor, especially 14 on the distortional ones, i.e., those that are not directly related to the variation of mass of 15 the body. The core message of our work is conceptual: we show that the growth laws usually 16 encountered in the literature, which are prescribed phenomenologically, but may be difficult to 17 justify theoretically, can be put in the framework of the Principle of Virtual Work by regarding 18 them as constraints. Moreover, we retrieve more particularized frameworks of growth available 19 in the literature, while being able to switch to a theory of growth of grade one, such as a Cahn-20 Hilliard model of growth. 21

23 Keywords

22

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

26 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

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

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

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

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

In our opinion, it is important to emphasize that, in those theories mentioned above, in which the PVW is used to study materials with microstructure, the PVW is formulated by extending 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

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

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

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

¹⁰¹ and rheonomic constraint on the growth tensor.

The just given interpretation of the mass balance constitutes the core of our present work. To 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].

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

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

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

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

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

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

¹⁴² **2** General Notation

In this section, we briefly give the notation used throughout the rest of our work. To this end, we introduce the three-dimensional Euclidean space \mathscr{S} , the reference placement of the body under study, i.e., $\mathscr{B} \subset \mathscr{S}$, the time line \mathscr{I} , the time interval $[t_{\rm in}, t_{\rm fin}] \subset \mathscr{I}$, and the map $\chi(\cdot, t) : \mathscr{B} \to \mathscr{S}$, which, for every time $t \in [t_{\rm in}, t_{\rm fin}] \subset \mathscr{I}$, transforms univocally each point X of \mathscr{B} into the point 147 $x = \chi(X,t) \in \mathscr{S}$, so that $\chi(\mathscr{B},t) =: \mathscr{B}_t \subset \mathscr{S}$ represents the change of shape of the body from 148 its reference placement to the placement \mathscr{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

$$\mathcal{X}: \mathscr{B} \times \mathscr{I} \to \mathscr{B}, \qquad \qquad \mathcal{X}(X, t) = X, \qquad (1a)$$

$$\mathcal{T}: \mathscr{B} \times \mathscr{I} \to \mathscr{I}, \qquad \qquad \mathcal{T}(X, t) = t \tag{1b}$$

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

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

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

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

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

We recall the BKL decomposition, $F(X,t) = F_{e}(X,t)K(X,t)$, where $F_{e}(X,t)$ and K(X,t) are 170 referred to as *tensor of elastic distortions* and *growth tensor*, respectively. The latter one, indeed, 171 describes the anelastic distortions induced in the body by the variation of mass due to growth. 172 For future use, we set $J := \det F$, $J_e := \det F_e$, and $J_K := \det K$. Here, we do not fuss over the 173 physical meanings attributed to the BKL decomposition, since a huge literature is available on the 174 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 175 mention that, although K is in principle a two-point tensor, in the sequel we consider it a mixed 176 tensor from $T_X \mathscr{B}$ into a "relaxed" copy of this vector space (see e.g. [28, 36]). 177

Finally, the maps \mathcal{X} and \mathcal{T} defined in Equations (1a) and (1b) are useful to express the explicit dependence of physical quantities on the points of \mathscr{B} and time. For instance, if h a is physical 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 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

In this section, we briefly review the mass balance law of the body under study in the context of the theory of volumetric growth based on the BKL decomposition. To this end, we recall that such decomposition permits to rewrite the balance of mass of the considered body as a relation between 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],

$$\operatorname{tr}(\boldsymbol{K}^{-1}\dot{\boldsymbol{K}}) \equiv \boldsymbol{K}^{-\mathrm{T}} : \dot{\boldsymbol{K}} = R_{\gamma}, \qquad \qquad \text{in } \mathscr{B} \times [t_{\mathrm{in}}, t_{\mathrm{fin}}], \qquad (3)$$

where R_{γ} is defined as $R_{\gamma} := Jr_{\gamma}/\rho_{\rm R}$, r_{γ} is the "true" source/sink of mass, and $\rho_{\rm R}$ is the mass density per unit volume of the body's reference placement. Equation (3) is obtained from the mass balance law, expressed in local form and with respect to the reference placement of the body, i.e., $\dot{\rho}_{\rm R} = Jr_{\gamma}$, by exploiting the relation $\rho_{\rm R} = J_{\mathbf{K}}\rho_{\nu}$, where ρ_{ν} is the mass density per unit volume of the body's natural state, and using the identity $\dot{J}_{\mathbf{K}} = J_{\mathbf{K}} \operatorname{tr}(\mathbf{K}^{-1}\dot{\mathbf{K}})$, under the hypothesis that ρ_{ν} is constant in time.

¹⁹³ We assume that R_{γ} is prescribed phenomenologically through a growth law of the type [100, 99]

$$R_{\gamma} \equiv R_{\gamma(\mathrm{ph})} := \bar{R}_{\gamma(\mathrm{ph})} \circ (\wp, \omega) = \hat{R}_{\gamma(\mathrm{ph})} \circ (\boldsymbol{F}, \boldsymbol{K}, \omega), \qquad \text{in } \mathscr{B} \times [t_{\mathrm{in}}, t_{\mathrm{fin}}], \qquad (4)$$

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

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

$$J_{\boldsymbol{K}}\varrho_{\nu}\dot{\omega} - \operatorname{Div}\left(J_{\boldsymbol{K}}\varrho_{\nu}\boldsymbol{D}\operatorname{Grad}\omega\right) = -J_{\boldsymbol{K}}\varrho_{\nu}r_{n}\omega - J_{\boldsymbol{K}}\varrho_{\nu}[\hat{R}_{\gamma(\mathrm{ph})}\circ(\boldsymbol{F},\boldsymbol{K},\omega)]\omega,\tag{5}$$

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

$$\omega = \omega_{\rm b}, \qquad \qquad \text{on } \partial_{\rm D}^{\omega} \mathscr{B}, \qquad (6a)$$

$$[-J_{\mathbf{K}}\varrho_{\nu}\boldsymbol{D}\operatorname{Grad}\omega]\boldsymbol{N} = \boldsymbol{j}_{\mathrm{b}},\qquad \qquad \text{on } \partial_{\mathrm{N}}^{\omega}\boldsymbol{\mathscr{B}},\qquad \qquad (6\mathrm{b})$$

$$\omega(X, t_{\rm in}) = \omega_{\rm in}(X), \qquad \qquad \text{in } \mathscr{B}, \qquad (6c)$$

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.

where $\omega_{\rm b}$ and $j_{\rm b}$ are the nutrients' mass fraction and flux imposed on the Dirichlet portion $\partial_{\rm D}^{\omega} \mathscr{B}$ and on the Neumann portion $\partial_{\rm N}^{\omega} \mathscr{B}$ of $\partial \mathscr{B}$ associated with ω , respectively.

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

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

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

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

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

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

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

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

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

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

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

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

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

where $S_{\gamma t}$ is one primitive of $R_{\gamma t}$ over $[t_{in}, t_{fin}]$, i.e., $\dot{S}_{\gamma t}(t) = R_{\gamma t}(t)$ for $t \in [t_{in}, t_{fin}]$, and f_0 is an arbitrary function of material points, only. Accordingly, Equation (10) can be rephrased as a holonomic constraint that prescribes $\check{f} \circ (\mathbf{K}, \mathcal{X}, \mathcal{T})$ to remain constant in time over $[t_{in}, t_{fin}]$. Moreover, since, without loss of generality, the constant value of $\check{f} \circ (\mathbf{K}, \mathcal{X}, \mathcal{T})$ can be assumed to be zero, the constraint becomes

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

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

$$\det \mathbf{K}(X,t) \equiv J_{\mathbf{K}}(X,t) = \exp\left(R_{\gamma p}(X)\int_{t_{\rm in}}^{t} R_{\gamma t}(s)\mathrm{d}s\right), \qquad \forall \ (X,t) \in \mathscr{B} \times [t_{\rm in}, t_{\rm fin}].$$
(12)

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

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

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

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

²⁵⁷ where we have exploited Equation (2b).

²⁵⁸ 4 Time as a constrained, fictitious Lagrangian parameter

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

²⁷⁵ $R_{\gamma(\text{ph})} \circ (\boldsymbol{F}, \boldsymbol{K}, \mathcal{X}, \mathcal{T})$, 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.

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

$$\mathfrak{T}: \mathscr{B} \times \mathscr{I} \to \mathscr{I}, \qquad \mathfrak{T}(X, t) = t_X.$$
 (14)

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 priori required to be equal to $t = \mathcal{T}(X, t)$, whereas the latter equality is true by definition.

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

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

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

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

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

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

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

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

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

Before going further, we notice that the constraint in Equation (13a), and, equivalently in Equation (13b), is linear in the rates $\dot{\mathbf{K}}$ and $\dot{\mathcal{T}}$. Thus, by recalling the definition of $\delta \mathcal{T}$, and introducing the virtual variation of the growth tensor $\delta \mathbf{K} : \mathscr{B} \times \mathscr{I} \to [T\mathscr{B}]^1$, where $[T\mathscr{B}]^1$ is the space of tensors mapping vectors of $T_X \mathscr{B}$ into vectors of $T_X \mathscr{B}$, we can rephrase Equation (13a) in the Lagrange-Chetaev form [95]⁵. This is obtained by replacing \dot{K} and $\dot{\mathcal{T}}$ with the "virtual displacements" δK and $\delta \mathcal{T}$, respectively, i.e.,

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

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

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

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

$$\hat{\mathcal{V}}_{\boldsymbol{K}} \circ (\boldsymbol{F}, \boldsymbol{K}, t_{c} \dot{\boldsymbol{K}}, t_{c} \dot{\boldsymbol{\mathfrak{T}}}, \omega) = t_{c} [\hat{\mathcal{V}}_{\boldsymbol{K}} \circ (\boldsymbol{F}, \boldsymbol{K}, \dot{\boldsymbol{\mathfrak{T}}}, \omega)] = 0,$$
(21)

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

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

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

thereby obtaining a constraint with the same physical dimensions as those in Equation (18b). We 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})

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

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 $[\partial_{\dot{\mathbf{K}}} \hat{\mathcal{V}} \circ (...)] : \delta \mathbf{K} + [\partial_{\dot{\mathfrak{T}}} \hat{\mathcal{V}} \circ (...)] \delta \mathfrak{T} = \mathbf{K}^{-\mathrm{T}} : \delta \mathbf{K} - [\hat{R}_{\gamma(\mathrm{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)] \delta \mathfrak{T} = 0.$

³³² useful to express the explicit time dependence of some physical quantities in a formally correct way.

Above all, the main reason for distinguishing between \mathfrak{T} and \mathcal{T} is the one that has been anticipated at the beginning of this section: since \mathfrak{T} is declared as a Lagrangian parameter, its virtual variation

at the beginning of this section: since \mathfrak{L} is declared as a Lagrangian parameter, its virtual variation $\delta \mathfrak{T}$ admits the introduction of fictitious forces, dual to $\delta \mathfrak{T}$, that produce virtual work on $\delta \mathfrak{T}$, and, 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 quantity $\mu_{\mathbf{K}}[\hat{R}_{\gamma(\mathrm{ph})} \circ (\mathbf{F}, \mathbf{K}, \omega)]$ or $\mu_{\mathbf{K}}[\check{R}_{\gamma(\mathrm{ph})} \circ (\mathbf{F}, \mathbf{K}, \mathcal{X}, \mathcal{T})]$, where $\mu_{\mathbf{K}}$ is the Lagrange multiplier associated with the constraint (20a), put in the form (19) (see Equation (24a) below).

³³⁹ 5 Principle of Virtual Work revisited

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

$$(\chi, \boldsymbol{F}, \boldsymbol{K}, \mathfrak{T}, \delta\chi, \operatorname{Grad}\delta\chi, \delta\boldsymbol{K}, \delta\mathfrak{T}).$$
 (23)

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

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

$$\delta \mu_{\boldsymbol{K}} \div [\hat{\mathcal{V}}_{\boldsymbol{K}} \circ (\boldsymbol{F}, \boldsymbol{K}, t_{c} \dot{\boldsymbol{K}}, t_{c} \dot{\boldsymbol{\mathfrak{T}}}, \omega)], \qquad \qquad \delta \mu_{\boldsymbol{\mathfrak{T}}} \div [\hat{\mathcal{V}}_{\boldsymbol{\mathfrak{T}}} \circ (t_{c} \dot{\boldsymbol{\mathfrak{T}}}, t_{c} \dot{\boldsymbol{\mathcal{T}}})], \qquad (24b)$$

 $_{349}$ where the symbol " \div " indicates the conjugation induced by duality.

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

$$\boldsymbol{P} \div \operatorname{Grad}\delta\chi, \quad \boldsymbol{Y}_{\mathrm{u}} \div \boldsymbol{K}^{-1}\delta\boldsymbol{K}, \quad \mathcal{Y}_{\mathrm{u}} \div \delta\mathfrak{T}, \tag{25}$$

where P is the "classical" first Piola-Kirchhoff stress tensor; $Y_{\rm u}$ is referred to as *internal growthconjugated stress* in the sequel, since it is a stress-like quantity dual to $K^{-1}\delta K$; and $\mathcal{Y}_{\rm u}$ is termed *internal time-conjugated force*, since it is dual to $\delta \mathfrak{T}$. The subscript "u" in $Y_{\rm u}$ and $\mathcal{Y}_{\rm u}$ indicates that these forces are "unconstrained", in the sense that, because of the presence of the Lagrangian multipliers μ_{K} and $\mu_{\mathfrak{T}}$, they are associated with arbitrary (and, thus, "unconstrained") variations δK and $\delta \mathfrak{T}$, respectively.

³⁵⁸ Finally, we consider the external generalized forces

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

where f and τ are the body forces per unit volume and the boundary contact forces per unit area of "classical" Continuum Mechanics, respectively, while, from here on, Z and Z are said to be *external growth-conjugated stress-like force*, and *external time-conjugated force*, respectively.

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

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

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

$$\int_{\mathscr{B}} \boldsymbol{P} : \operatorname{Grad}\delta\chi + \int_{\mathscr{B}} \boldsymbol{Y}_{u} : \boldsymbol{K}^{-1}\delta\boldsymbol{K} + \int_{\mathscr{B}} \mathcal{Y}_{u}\delta\mathfrak{T} \\
+ \int_{\mathscr{B}} \mu_{\boldsymbol{K}}[\hat{\mathcal{V}}_{\boldsymbol{K}} \circ (\boldsymbol{F}, \boldsymbol{K}, \delta\boldsymbol{K}, \delta\boldsymbol{T}, \omega)] + \int_{\mathscr{B}} \mu_{\mathfrak{T}}[\hat{\mathcal{V}}_{\mathfrak{T}} \circ (\delta\mathfrak{T}, \delta\boldsymbol{T})] \\
+ \int_{\mathscr{B}} \delta\mu_{\boldsymbol{K}}[\hat{\mathcal{V}}_{\boldsymbol{K}} \circ (\boldsymbol{F}, \boldsymbol{K}, t_{c}\dot{\boldsymbol{K}}, t_{c}\dot{\mathfrak{T}}, \omega)] + \int_{\mathscr{B}} \delta\mu_{\mathfrak{T}}[\hat{\mathcal{V}}_{\mathfrak{T}} \circ (t_{c}\dot{\mathfrak{T}}, t_{c}\dot{\boldsymbol{T}})] \\
= \int_{\mathscr{B}} \boldsymbol{f}\delta\chi + \int_{\partial_{N}^{\chi}\mathscr{B}} \boldsymbol{\tau}\delta\chi + \int_{\mathscr{B}} \boldsymbol{Z} : \boldsymbol{K}^{-1}\delta\boldsymbol{K} + \int_{\mathscr{B}} \mathcal{Z}\delta\mathfrak{T}, \qquad (27)$$

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

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

³⁸¹ 5.1 Dynamic equations in local form

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 $\hat{\mathcal{V}}_{\mathfrak{T}} \circ (\delta \mathfrak{T}, \delta \mathcal{T})$, Equation (27) can be recast in the form

$$\int_{\partial_{\mathbf{N}}^{\mathfrak{X}}\mathscr{B}} \{\boldsymbol{\tau} - \boldsymbol{P}\boldsymbol{N}\} \delta \chi + \int_{\mathscr{B}} \{\operatorname{Div}\boldsymbol{P} + \boldsymbol{f}\} \delta \chi$$

$$+ \int_{\mathscr{B}} \{\boldsymbol{Z} - \mu_{\boldsymbol{K}}\boldsymbol{I}^{\mathrm{T}} - \boldsymbol{Y}_{\mathrm{u}}\} : \boldsymbol{K}^{-1} \delta \boldsymbol{K} + \int_{\mathscr{B}} \{\mathcal{Z} - \mathcal{Y}_{\mathrm{u}} - \mu_{\mathfrak{T}}\} \delta \mathfrak{T}$$

$$+ \int_{\mathscr{B}} \{\mu_{\boldsymbol{K}}[\hat{R}_{\gamma(\mathrm{ph})} \circ (\boldsymbol{F}, \boldsymbol{K}, \omega)] + \mu_{\mathfrak{T}}\} \delta \mathcal{T}$$

$$- \int_{\mathscr{B}} \delta \mu_{\boldsymbol{K}}[\hat{\mathcal{V}}_{\boldsymbol{K}} \circ (\boldsymbol{F}, \boldsymbol{K}, t_{\mathrm{c}} \dot{\boldsymbol{K}}, t_{\mathrm{c}} \dot{\mathfrak{T}}, \omega)] - \int_{\mathscr{B}} \delta \mu_{\mathfrak{T}}[\hat{\mathcal{V}}_{\mathfrak{T}} \circ (t_{\mathrm{c}} \dot{\mathfrak{T}}, t_{\mathrm{c}} \dot{\mathcal{T}})] = 0, \qquad (28)$$

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

$\mathrm{Div}\boldsymbol{P}+\boldsymbol{f}=\boldsymbol{0},$	$ \text{in} \ \mathscr{B},$	(29a)
$\chi = \chi_{\rm b},$	on $\partial_{\mathrm{D}}^{\chi} \mathscr{B}$,	(29b)
$PN = \tau$,	on $\partial_{\mathbf{N}}^{\chi} \mathscr{B}$,	(29c)
$\left(\boldsymbol{Y}_{\mathrm{u}} + \mu_{\boldsymbol{K}} \boldsymbol{I}^{\mathrm{T}} \right) - \boldsymbol{Z} = \boldsymbol{0},$	$ \text{in} \ \mathscr{B},$	(29d)
$(\mathcal{Y}_{\mathrm{u}} + \mu_{\mathfrak{T}}) - \mathcal{Z} = 0,$	$ \text{in} \ \mathscr{B},$	(29e)
$\mu_{\boldsymbol{K}}[\hat{R}_{\gamma(\mathrm{ph})}\circ(\boldsymbol{F},\boldsymbol{K},\omega)]+\mu_{\mathfrak{T}}=0,$	$ \text{in} \ \mathscr{B},$	(29f)
$\hat{\mathcal{V}}_{\boldsymbol{K}} \circ (\boldsymbol{F}, \boldsymbol{K}, t_{c} \dot{\boldsymbol{K}}, t_{c} \dot{\boldsymbol{\mathfrak{T}}}, \omega) = 0,$	$ \text{in} \ \mathscr{B},$	(29g)
$\hat{\mathcal{V}}_{\mathfrak{T}} \circ (t_c \dot{\mathfrak{T}}, t_c \dot{\mathcal{T}}) = 0,$	in \mathscr{B} .	(29h)

Equation (29a) is the local form of the balance of linear momentum of "classical" Continuum Mechanics, equipped with the Dirichlet boundary condition (29b) and the Neumann boundary condition (29c), where $\chi_{\rm b}$ is the motion prescribed on $\partial_{\rm D}^{\chi} \mathscr{B}$, and N is the field of co-normals defined over $\partial \mathscr{B}$.

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

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

After the constitutive framework is established, Equations (29a) and (29d)–(29h) constitute a set of 16 scalar equations in the unknowns χ , K, μ_K , $\mu_{\mathfrak{T}}$, $\mathcal{Z} - \mathcal{Y}_u$, and \mathfrak{T} , which amount to 16 scalar unknowns. Hence, the problem is closed. In particular, Equation (29g) allows to determine the Lagrange multiplier $\mu_{\mathbf{K}}$ (although, given the specific hypotheses adopted in this work, a different procedure will be used in the sequel), while Equation (29h) is used to obtain $\mathfrak{T}(X,t) = t$, so that the Lagrange multiplier $\mu_{\mathfrak{T}}$ is determined by means of Equation (29f). In our opinion, the constraint on time constitutes a novelty in our approach, since it has not been considered in the previous formulations of growth which we are aware of.

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

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

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

$$\mathcal{Y}_{u} + \mu_{\mathfrak{T}} = \mathcal{Z},$$
 in $\mathscr{B},$ (30a)

$$\mu_{\mathfrak{T}} = -\mu_{\boldsymbol{K}}[\hat{R}_{\gamma(\mathrm{ph})} \circ (\boldsymbol{F}, \boldsymbol{K}, \omega)], \qquad \text{in } \mathscr{B}, \qquad (30b)$$

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

$$\mathcal{Z} - \mathcal{Y}_{u} = \mu_{\mathfrak{T}} = -\mu_{\boldsymbol{K}}[\hat{R}_{\gamma(\mathrm{ph})} \circ (\boldsymbol{F}, \boldsymbol{K}, \omega)], \qquad \text{in } \mathscr{B}.$$
(31)

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

$$\boldsymbol{Y}_{u} + \boldsymbol{\mu}_{\boldsymbol{K}} \boldsymbol{I}^{\mathrm{T}} - \boldsymbol{Z} = \boldsymbol{0}, \qquad \qquad \text{in } \mathscr{B}, \qquad (32a)$$

$$\boldsymbol{K}^{-\mathrm{T}}: \boldsymbol{K} - \hat{R}_{\gamma(\mathrm{ph})} \circ (\boldsymbol{F}, \boldsymbol{K}, \omega) = 0, \qquad \text{in } \mathscr{B}. \tag{32b}$$

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

$$\operatorname{dev} \boldsymbol{Y}_{\mathrm{u}} = \operatorname{dev} \boldsymbol{Z}, \qquad \qquad \text{in } \mathcal{B}, \qquad (33a)$$

$$\boldsymbol{K}^{-\mathrm{T}}: \dot{\boldsymbol{K}} = \hat{R}_{\gamma(\mathrm{ph})} \circ (\boldsymbol{F}, \boldsymbol{K}, \omega), \qquad \text{in } \mathscr{B}, \qquad (33b)$$

$$\mu_{\boldsymbol{K}} = \frac{1}{3} \text{tr} \boldsymbol{Z} - \frac{1}{3} \text{tr} \boldsymbol{Y}_{u}, \qquad \text{in } \mathscr{B}. \qquad (33c)$$

Now, if Z is supplied through a function independent of \dot{K} and other time derivatives of K of order higher than the first, and if Y_{u} is expressed constitutively as a function of K and \dot{K} , then Equations (33a) and (33b) become a set of first-order ordinary differential equations. Thus, once Z is assigned and Y_{u} is provided constitutively, the Lagrangian multiplier μ_{K} is determined by the right-hand-side of Equation (33c), while Equations (33a) and (33b) are sufficient to determine the 9 independent components of K. Therefore, the boundary value problem that has to be solved ⁴⁴² according to the formulation presented in this work is given by

$$\operatorname{Div} \boldsymbol{P} + \boldsymbol{f} = \boldsymbol{0}, \qquad \qquad \text{in } \mathscr{B}, \qquad (34a)$$

(0.41

$$\chi = \chi_{\rm b}, \qquad \text{on } \partial_{\rm D}^{\chi} \mathscr{B}, \qquad (34b)$$
$$\mathbf{PN} = \boldsymbol{\tau}. \qquad \text{on } \partial_{\rm N}^{\chi} \mathscr{B}. \qquad (34c)$$

$$\boldsymbol{K}^{-\mathrm{T}}: \dot{\boldsymbol{K}} = \hat{R}_{\gamma(\mathrm{ph})} \circ (\boldsymbol{F}, \boldsymbol{K}, \omega), \qquad \text{in } \mathscr{B}, \qquad (34e)$$

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

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

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

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

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

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

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

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

490 6.1 Local dissipation

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

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

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

$$\mathcal{D}_{\mathrm{R}} = -\dot{\Psi}_{\mathrm{R}} + \boldsymbol{P} : \boldsymbol{\dot{F}} + \boldsymbol{Y}_{\mathrm{u}} : \boldsymbol{K}^{-1} \boldsymbol{\dot{K}} \ge 0.$$
(37)

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

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

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

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

where H is Eshelby stress tensor, and $Y_{u,d}$ is the *dissipative part* of Y_u (see also [24, 38, 37]), the dissipation inequality reduces to

$$\mathcal{D}_{\mathrm{R}} = \boldsymbol{Y}_{\mathrm{u,d}} : \boldsymbol{K}^{-1} \dot{\boldsymbol{K}} \ge 0.$$
(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 $Y_{u,d}$ by using a decomposition of fourth-order tensors [108] that yields (see also ⁵⁰⁶ [70, 64, 94])

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

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

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

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

521 6.3 Final form of the IBVP

In summary, the set of equations describing the considered growing medium consists of Equation (34a), i.e., the linear momentum balance law, which determines the medium's deformation, χ ; Equations (34d), i.e., the balance of forces dual to the unconstrained part of \dot{K} ; Equation (34e), i.e., the constraint describing the medium's growth; Equation (5), which represents the diffusionreaction equation for the nutrients' mass fraction, ω . The above mentioned list of equations is equipped with the boundary conditions (34b) and (34c), assessing prescribed deformations and 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].

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

$\operatorname{Div} \boldsymbol{P} = -\boldsymbol{f},$	in \mathscr{B} ,	(42a)
$\chi=\chi_{ m b},$	on $\partial_{\mathbf{D}}^{\chi} \mathscr{B}$,	(42b)
$oldsymbol{PN}=oldsymbol{ au},$	on $\partial_{\mathbf{N}}^{\chi} \mathscr{B}$,	(42c)
$2J_{\boldsymbol{K}}\mathfrak{b}_{\nu}\mathrm{dev}_{\boldsymbol{C}}\mathrm{sym}[(\boldsymbol{K}^{-1}\dot{\boldsymbol{K}})\boldsymbol{C}^{-1}] = -\boldsymbol{C}^{-1}\mathrm{dev}\boldsymbol{H} + \boldsymbol{C}^{-1}\mathrm{dev}\boldsymbol{Z},$	in \mathscr{B} ,	(42d)
$2J_{\boldsymbol{K}}\mathfrak{c}_{\nu}\mathrm{skew}[(\boldsymbol{K}^{-1}\dot{\boldsymbol{K}})\boldsymbol{C}^{-1}] = \boldsymbol{0},$	in \mathscr{B} ,	(42e)
$\boldsymbol{K}^{-\mathrm{T}}: \dot{\boldsymbol{K}} = R_{\gamma(\mathrm{ph})},$	in \mathscr{B} ,	(42f)
$\boldsymbol{K}(X, t_{\rm in}) = \boldsymbol{K}_{\rm in}(X),$	in \mathscr{B} ,	(42g)
$J_{\mathbf{K}}\varrho_{\nu}\dot{\omega} - \operatorname{Div}(J_{\mathbf{K}}\varrho_{\nu}\boldsymbol{D}\operatorname{Grad}\omega) = -J_{\mathbf{K}}\varrho_{\nu}r_{n}\omega - J_{\mathbf{K}}\varrho_{\nu}R_{\gamma(\mathrm{ph})}\omega,$	$ \text{in} \ \mathscr{B},$	(42h)
$\omega = \omega_{ m b},$	on $\partial_{\mathbf{D}}^{\omega}\mathscr{B}$,	(42i)
$[-J_{\boldsymbol{K}}\varrho_{\boldsymbol{\nu}}\boldsymbol{D}\operatorname{Grad}\omega]\boldsymbol{N}=\jmath_{\mathrm{b}},$	on $\partial_{\mathbf{N}}^{\omega}\mathscr{B}$,	(42j)
$\omega(X, t_{\rm in}) = \omega_{\rm in}(X),$	$ \text{in} \ \mathscr{B},$	(42k)

where the operator dev_C is defined by dev_C $T := T - \frac{1}{3}$ tr(CT) C^{-1} , for all second-order, contravariant tensors T. Note that Equations (42d) and (42e) are obtained by left-multiplying Equation (34d) by C^{-1} , employing Equation (40) for the constitutive representation of Y_{u} , and extracting once the symmetric part and once the skew-symmetric part of the resulting expression. Moreover, we remark that Equation (42d) is equivalent to

$$J_{\boldsymbol{K}}\mathfrak{b}_{\nu}\operatorname{dev}\{\boldsymbol{C}\boldsymbol{K}^{-1}\dot{\boldsymbol{K}}\boldsymbol{C}^{-1}+(\boldsymbol{K}^{-1}\dot{\boldsymbol{K}})^{\mathrm{T}}\}=-\operatorname{dev}\boldsymbol{H}+\operatorname{dev}\boldsymbol{Z},\qquad \text{in }\mathscr{B}.$$
 (43)

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

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

$$(44a)$$

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

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

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

(44b)

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

542 6.4 The limit case of spherical growth tensor

In several problems addressing the growth of a tumor in the so-called "avascular stage" [25], the growth tensor is often assumed to be spherical from the outset [9, 11, 100, 59, 58]. By considering 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 study incompressibility in finite deformations), which implies det $\mathbf{K} = J_{\mathbf{K}}$ and, thus, necessarily det $\tilde{\mathbf{K}} = 1$, the hypothesis of spherical growth tensor amounts to set $\tilde{\mathbf{K}} = \mathbf{I}$ and, thus, $\mathbf{K} = J_{\mathbf{K}}^{1/3}\mathbf{I}$. Consequently, \mathbf{K} features one free component only, i.e., $J_{\mathbf{K}}$, which, in turn, is restricted by Equation (3) to fulfill the constraint

$$\dot{J}_{\boldsymbol{K}} = R_{\gamma(\mathrm{ph})} J_{\boldsymbol{K}},\tag{46}$$

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

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

$$(y_{\mathbf{u}} + \boldsymbol{\mu}_{\boldsymbol{K}}) - z = 0, \tag{47}$$

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

$$\mu_{\boldsymbol{K}} = z - y_{\mathbf{u}},\tag{48}$$

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

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

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

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

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

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

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

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

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

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

$$\frac{J_{\boldsymbol{K}}}{J_{\boldsymbol{K}}} = -\frac{1}{J_{\boldsymbol{K}}} \operatorname{Div} \boldsymbol{v} + R_{\gamma(\mathrm{ph})}, \tag{52}$$

with $\mathbf{v} := \varrho_{\nu}^{-1} \mathfrak{I}_{\mathrm{R}}$ being a normalized mass flux vector having physical dimensions of velocity.

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

$$-\operatorname{Div}\boldsymbol{\xi} + \pi = \gamma, \qquad \qquad \text{work-conjugate with } \delta\varrho_{\mathrm{R}} \text{ (see [74])}, \qquad (53a)$$

$$-\operatorname{Div}\mathfrak{f} + \left(\mathfrak{f}\frac{\operatorname{Grad}J_{\boldsymbol{K}}}{J_{\boldsymbol{K}}} + q_{\mathrm{u}} + \mu_{\boldsymbol{K}}\right) = z, \qquad \text{work-conjugate with } \frac{\delta J_{\boldsymbol{K}}}{J_{\boldsymbol{K}}}.$$
(53b)

Thus, a comparison of Equation (53b) with Equation (47) allows to identify the internal generalized force $y_{\rm u}$ with the combination

$$y_{\rm u} \equiv -\text{Div}\mathfrak{f} + \left(\mathfrak{f}\frac{\text{Grad}J_{\mathbf{K}}}{J_{\mathbf{K}}} + q_{\rm u}\right) = -\text{Div}\mathfrak{f} + q_{\rm u,eff},\tag{54a}$$

$$q_{\rm u,eff} := \mathfrak{f} \frac{\mathrm{Grad}J_{\mathbf{K}}}{J_{\mathbf{K}}} + q_{\rm u},\tag{54b}$$

where $q_{\rm u}$ is the generalized internal force associated with growth, while $q_{\rm u,eff}$ describes an *effective internal force*, in which the term $\mathbf{f}J_{\mathbf{K}}^{-1}$ Grad $J_{\mathbf{K}}$ accounts for the inhomogeneity of $J_{\mathbf{K}}$, and is indeed remnant of the "inhomogeneity force" introduced by Epstein and Maugin [41] in the context of growth mechanics (see also [101] for a more general context). We remark that Equations (53a) and (53b) can be found by adapting the PVW in Equation (27) to a theory of grade one in $J_{\mathbf{K}}$. This, in general, also requires prescribing $\mathbf{f}N$ on the portions of $\partial \mathscr{B}$ on which contact forces dual to $\delta J_{\mathbf{K}}/J_{\mathbf{K}}$, or to $\delta \varrho_{\rm R}$, 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].

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

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

$$\mathbf{\mathfrak{f}} \equiv \varrho_{\mathrm{R}} \boldsymbol{\xi},\tag{55a}$$

$$q_{\rm u} + \mu_{\boldsymbol{K}} \equiv \varrho_{\rm R} \pi, \tag{55b}$$

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

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).

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

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

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

$$\int_{\mathscr{R}} \mathcal{D}_{\mathrm{R,new}} = \int_{\mathscr{R}} \mathcal{D}_{\mathrm{R,old}} + \int_{\partial \mathscr{R}} \mathfrak{f}[\dot{J}_{\boldsymbol{K}}/J_{\boldsymbol{K}}] \boldsymbol{N} - \int_{\partial \mathscr{R}} \mu_{\mathrm{ch}} J_{\boldsymbol{K}}^{-1} \mathfrak{v} \boldsymbol{N} \ge 0,$$
(56)

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

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

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

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

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

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

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

$$\mathcal{D}_{\mathrm{R,new}} = q_{\mathrm{u,d}} J_{\boldsymbol{K}}^{-1} \dot{J}_{\boldsymbol{K}} + \mathfrak{v} \operatorname{Grad}(J_{\boldsymbol{K}}^{-1} \mu_{\boldsymbol{K}}) \ge 0,$$
(59)

646 which allows to take

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

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

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

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

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

⁶⁵² where we introduced the notation

$$\mathcal{E}_{J_{\boldsymbol{K}}}\Psi_{\mathrm{R}} := \frac{\partial \hat{\Psi}_{\mathrm{R}}}{\partial J_{\boldsymbol{K}}} \circ (\boldsymbol{F}, J_{\boldsymbol{K}}, \mathrm{Grad}J_{\boldsymbol{K}}) - \mathrm{Div} \bigg[\frac{\partial \hat{\Psi}_{\mathrm{R}}}{\partial \mathrm{Grad}J_{\boldsymbol{K}}} \circ (\boldsymbol{F}, J_{\boldsymbol{K}}, \mathrm{Grad}J_{\boldsymbol{K}}) \bigg].$$
(62)

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

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

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

655 8 Conclusions

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

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

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

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

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

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

⁶⁹⁴ Remark 8.2 (The case of vanishing $tr Y_{u,d}$)

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

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

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

• The case of no growth (see Remark 8.1) trivially restricts $J_{\mathbf{K}}$ to remain equal to its initial distribution, $J_{\mathbf{K}}^{\text{in}}$, while $\mu_{\mathbf{K}}$ becomes $\mu_{\mathbf{K}} = z - J_{\mathbf{K}}^{\text{in}}[\partial_{J_{\mathbf{K}}}\hat{\Psi}_{\mathrm{R}} \circ (\mathbf{F}, J_{\mathbf{K}}^{\text{in}})]$, with z being possibly null. The quantity $J_{\mathbf{K}}^{\text{in}}$, in fact, need not be unitary, in general, because the "initial" state of the body may coincide with a state in which growth has occurred and has then come to a stop (see e.g. [36]). Clearly, also in this case, no growth implies the vanishing of $y_{\mathrm{u,d}}$, whereas the vice versa, in general, does not apply.

• The discussion done in Remark 8.2 on the vanishing of $y_{u,d}$ is recovered for $\kappa_{\nu} = 0$, thereby yielding $y_u = J_{\boldsymbol{K}}[\partial_{J_{\boldsymbol{K}}}\hat{\Psi}_{\mathrm{R}} \circ (\boldsymbol{F}, J_{\boldsymbol{K}})]$, and $\mu_{\boldsymbol{K}} = z - J_{\boldsymbol{K}}[\partial_{J_{\boldsymbol{K}}}\hat{\Psi}_{\mathrm{R}} \circ (\boldsymbol{F}, J_{\boldsymbol{K}})]$, while the evolution of $J_{\boldsymbol{K}}$ remains prescribed by Equation (46).

717 8.2 Main results within the Cahn-Hilliard theory

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

⁷²⁷ Remark 8.3 (Vanishing $R_{\gamma(ph)}$ and vanishing $q_{u,d}$ within the Cahn-Hilliard approach)

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

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.,

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

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

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

746 8.3 Connections with other theories of growth

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

751 8.3.1 Growth viewed as a "flow rule".

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

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

As anticipated in the Introduction, DiCarlo and Quiligotti [38] formulate a model of growth whose ref core is the balance of the stress-like forces dual to the virtual variations of 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].

force balance is obtained without any *a priori* constraint on the growth tensor or its rate, and, 768 after establishing the constitutive framework and studying the system's dissipation inequality, it is 769 written as $Y_{d} + H = Z$ (in our notation), where Y_{d} is the dissipative part of the overall generalized 770 internal force Y (compare with our Equation (29d)). This way, DiCarlo and Quiligotti [38] highlight 771 the interaction between Eshelby stress tensor H and the stress-like generalized force Y (" $-\mathbb{C}$ " in 772 their notation). This interaction, referred to as "Eshelbian coupling" by DiCarlo and Quiligotti 773 [38], is mentioned also by DiCarlo [37] in conjunction with the role attributed to the generalized 774 force Z (" \mathbb{B} " in his notation). Indeed, by rephrasing DiCarlo's words [37], one may say that Z775 resolves the biochemical interactions that, possibly occurring at different scales, promote or hinder 776 the growth of a biological system, and models their influence on the mechanics of the system's 777 structural evolution at the continuum scale. Thus, if we correctly interpret DiCarlo's thoughts 778 [37], it is hard to construct a biologically consistent mechanical theory of growth without \mathbf{Z} , since 779 Eshelby stress tensor alone is unable to capture the necessary biological information that guides 780 growth. This, in turn, contrasts with the model of growth provided by Epstein and Maugin [41]. 781

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

809 8.3.3 Towards a unified approach to inelastic processes.

As a final remark, let us notice that, since our approach is based on a growth law given a priori, 810 the variation of mass considered in our work need not be correlated, in principle, with any measure 811 of stress, although we do let $R_{\gamma(ph)}$ depend on \wp , as reported in Equation (4). This fact emphasizes 812 that the constrained approach, although being constrained, guarantees a certain freedom in the 813 choice of the growth law; a freedom that is balanced by the restrictions placed on tensor K. In 814 this respect, however, we think that our approach may be used also in physical situations deeply 815 different from growth, in which it is anyway necessary, or preferable, to assign the evolution of 816 K a priori. Indeed, as an outlook for future research, we have in mind to reformulate in the 817 context of growth and/or remodeling some models of the inelastic phenomena taken from the 818 literature, like, for instance, Gurtin's constrained plasticity [71, 72, 73], or the plastic flow rules 819 suggested by Mićunović [102], and obtained experimentally for the case of non-associative plasticity. 820 Furthermore, a natural extension of a theory of growth of grade one in the inelastic variable K821 would consist in switching to constitutive relations of grade two in the deformation. Although such 822 approaches, in fact, have been proposed for the case of bone remodeling by adopting linear energy 823 densities (see e.g. [54]), the framework of growth might call for the generalization of these energies 824 to the nonlinear case. 825

⁸²⁶ Conflict of Interests

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

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⁸⁴² A1: Time as a fictitious, additional Lagrangian parameter

To explain the reasons for regarding time as a fictitious, additional Lagrangian parameter of the problem under investigation, let us briefly review the approach of Analytical Mechanics to a generic discrete mechanical system [17] subjected to non-holonomic and rheonomic constraints [87]. To this end, let us consider a system of this type, described by $n \ge 1$, $n \in \mathbb{N}$, free generalized coordinates, which, as is customary in Analytical Mechanics, are denoted by q^1, \ldots, q^n . For each $k = 1, \ldots, n$, let $q^k : [t_{\text{in}}, t_{\text{fin}}] \to \mathbb{R}$ be a function of time fulfilling all the differentiability hypotheses that are necessary for the forthcoming discussion. Let us also consider $m \in \mathbb{N}$, $m \le n$, linearly independent, non-holonomic and rheonomic constraints, i.e., restrictions on the generalized velocities $\dot{q}^1, \ldots, \dot{q}^n$ that, under the hypotheses of linearity in $\dot{q}^1, \ldots, \dot{q}^n$, can be expressed as

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

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

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

On the other hand, if the constraints (65) are accounted for through the method of Lagrange 865 multipliers, framed within the context of the Principle of Virtual Work, the coefficients $b^i(q(t),t)$ 866 necessitate a dedicated study. Indeed, since they are not multiplied by any virtual displacement, 867 they spoil the standard procedure on which the Principle of Virtual Work is based. To see this, let us 868 define the virtual displacements $\delta q^1, \ldots, \delta q^n$, and let us recall that, at each fixed time $t \in [t_{\text{in}}, t_{\text{fin}}]$, 869 and for each k = 1, ..., n, the symbol $\delta q^k(t)$ represents a virtual variation of the value taken by q^k 870 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 871 of the system's global configuration at time t, i.e., q(t), and the corresponding virtual work can be 872 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 $\delta q^k(t)^9$. Granted this background, as suggested by Lanczos [87], the constraints (65) can be reformulated 873

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

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

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

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

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

none of those features the variation $\delta t(t)$. To solve this problem, we proceed in two steps. First, we introduce the fictitious Lagrangian parameter $\mathfrak{T} : \mathscr{I} \to \mathscr{I}$, such that $\mathfrak{T}(t) = t_0 + t$, where $t_0 \in \mathscr{I}$ is a given constant. We say that the map \mathfrak{T} is a "fictitious Lagrangian parameter" because its evolution is already prescribed and is consistent with the transformation of time of Galileian mechanics, thereby yielding the condition $\dot{\mathfrak{T}}(t) = 1$, for all $t \in \mathscr{I}$. This condition, in fact, can be regarded as an additional constraint, and is satisfied as $\delta \mathfrak{T}(t) = \delta t(t)$, when it is written in terms of the virtual variation of \mathfrak{T} at t, denoted by $\delta \mathfrak{T}(t)$.

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

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

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

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

⁸⁹⁴ and leads to the system of equations

$$Q_k(t) + \sum_{i=1}^m \mu_i[a_k^i(q(t), t)] = 0, \qquad k = 1, \dots, n,$$
(69a)

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

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

which, in conjunction with Equation (65), allow to determine the *n* Lagrangian parameters q^1, \ldots, q^n , the *m* Lagrange multipliers μ_1, \ldots, μ_m , as well as $\mu_{\mathfrak{T}}$ and $\mathcal{Q}_{\mathfrak{T}}$. Note that, for brevity, in equations (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 $t_c > 0$ being a characteristic time. These terms, however, are identically zero.

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

In this section, we sketch the main changes that take place in the procedure shown in section 6, if the hypothesis concerning the vanishing of Z is relaxed and, rather, 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

$$\int_{\mathscr{R}} \mathcal{D}_{\mathrm{R}} = \int_{\mathscr{R}} \mathcal{D}_{\mathrm{R,old}} + \int_{\mathscr{R}} \mathcal{Z} \dot{\mathfrak{T}} - \int_{\mathscr{R}} \mu_{\mathfrak{T}} \dot{\mathcal{T}} \ge 0, \tag{70}$$

where $\int_{\mathscr{R}} \mathcal{D}_{\mathrm{R,old}}$ coincides with the right-hand side of Equation (35), with $\mu_{\mathrm{ch}} \equiv -\mu_{\mathbf{K}}$, the term $\mathcal{Z}\hat{\mathfrak{T}}$ 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 summand on the right-hand side of Equation (35) to account for the fact that $\dot{\mathfrak{T}}$ is constrained to 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 the same localization procedure that has led to Equation (37) from Equation (35), recalling the force balance $\mathcal{Y}_{\mathrm{u}} + \mu_{\mathfrak{T}} = \mathcal{Z}$ of Equation (29e), and enforcing the constraint $\dot{\mathfrak{T}} = \dot{\mathcal{T}}$, we obtain now

$$\mathcal{D}_{\mathrm{R}} = -\dot{\Psi}_{\mathrm{R}} + \boldsymbol{P} : \dot{\boldsymbol{F}} + \boldsymbol{Y}_{\mathrm{u}} : \boldsymbol{K}^{-1} \dot{\boldsymbol{K}} + \mathcal{Y}_{\mathrm{u}} \dot{\boldsymbol{\mathfrak{I}}} \ge 0.$$
(71)

Thus, under the constitutive hypotheses presented in section 6.1, which declare $\hat{\Psi}_{R}$ as independent 910 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 911 from the identity $\dot{\mathcal{T}}(X,t) = 1$), we conclude that the condition $\mathcal{Y}_{u} = 0$ must hold, and, thus, that 912 Equation (71) yields Equation (39), i.e., $\mathcal{D}_{\mathrm{R}} = Y_{\mathrm{u,d}} : \mathbf{K}^{-1}\mathbf{K} \geq 0$. Hence, the study of the residual 913 dissipation inequality, the solution of the IBVP (42a)-(42k), and the a posteriori determination of 914 $\mu_{\mathbf{K}}$ and $\mu_{\mathfrak{T}}$ as shown in Equations (44a) and (44b) can proceed as shown in the main body of our 915 work. However, the difference with respect to the model presented above is that Equation (29e) 916 now determines \mathcal{Z} , because \mathcal{Y}_{u} vanishes for constitutive reasons, so that Equations (31) and (45) 917 now become 918

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

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

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