

An asymptotic homogenization approach to the microstructural evolution of heterogeneous media

*Original*

An asymptotic homogenization approach to the microstructural evolution of heterogeneous media / Ramírez-Torres, Ariel; Di Stefano, Salvatore; Grillo, Alfio; Rodríguez-Ramos, Reinaldo; Merodio, José; Penta, Raimondo. - In: INTERNATIONAL JOURNAL OF NON-LINEAR MECHANICS. - ISSN 0020-7462. - 106:(2018), pp. 245-257. [10.1016/j.ijnonlinmec.2018.06.012]

*Availability:*

This version is available at: 11583/2720458 since: 2020-06-03T17:41:57Z

*Publisher:*

Elsevier Ltd

*Published*

DOI:10.1016/j.ijnonlinmec.2018.06.012

*Terms of use:*

This article is made available under terms and conditions as specified in the corresponding bibliographic description in the repository

*Publisher copyright*

Elsevier postprint/Author's Accepted Manuscript

© 2018. This manuscript version is made available under the CC-BY-NC-ND 4.0 license  
<http://creativecommons.org/licenses/by-nc-nd/4.0/>. The final authenticated version is available online at:  
<http://dx.doi.org/10.1016/j.ijnonlinmec.2018.06.012>

(Article begins on next page)

1 An Asymptotic Homogenization Approach to the  
2 Microstructural Evolution of Heterogeneous Media

3 Ariel Ramírez-Torres<sup>a</sup>, Salvatore Di Stefano<sup>a</sup>, Alfio Grillo<sup>a</sup>,  
4 Reinaldo Rodríguez-Ramos<sup>b</sup>, José Merodio<sup>c</sup>, Raimondo Penta<sup>d,\*</sup>

5 <sup>a</sup>*Dipartimento di Scienze Matematiche “G. L. Lagrange”,*  
6 *Politecnico di Torino, Torino, 10129, Italy*

7 <sup>b</sup>*Departamento de Matemáticas, Facultad de Matemática y Computación,*  
8 *Universidad de La Habana, La Habana, CP 10400, Cuba*

9 <sup>c</sup>*Departamento de Mecánica de los Medios Continuos y T. Estructuras,*  
10 *E.T.S. de Caminos, Canales y Puertos,*  
11 *Universidad Politécnica de Madrid, Madrid, CP 28040, Spain*

12 <sup>d</sup>*School of Mathematics and Statistics, Mathematics and Statistics Building,*  
13 *University of Glasgow, University Place, Glasgow G12 8QQ, UK*

---

14 **Abstract**

In the present work, we apply the asymptotic homogenization technique to the equations describing the dynamics of a heterogeneous material with evolving micro-structure, thereby obtaining a set of upscaled, effective equations. We consider the case in which the heterogeneous body comprises two hyperelastic materials and we assume that the evolution of their micro-structure occurs through the development of plastic-like distortions, the latter ones being accounted for by means of the Bilby-Kröner-Lee (BKL) decomposition. The asymptotic homogenization approach is applied simultaneously to the linear momentum balance law of the body and to the evolution law for the plastic-like distortions. Such evolution law models a stress-driven production of inelastic distortions, and stems from phenomenological observations done on cellular aggregates. The whole study is also framed within the limit of small elastic distortions, and provides a robust framework that can be readily generalized to growth and remodeling of nonlinear composites. Finally, we complete our theoretical model by performing numerical simulations.

15 *Keywords:* Asymptotic homogenization, heterogeneous media, remodeling,  
16 BKL decomposition, two-scale plasticity, nonlinear composites

---

\*Corresponding author

*Email address:* [raimondo.penta@glasgow.ac.uk](mailto:raimondo.penta@glasgow.ac.uk) (Raimondo Penta)

17 **1. Introduction**

18 The study of material growth, remodeling and aging is of great impor-  
19 tance in Biomechanics, specially when the tissue, in which these processes  
20 occur, features a very complex structure, with different scales of observation  
21 and various constituents.

22 In the literature, the study of heterogeneous materials follows several  
23 approaches. In this work we focus on the multi-scale asymptotic homoge-  
24 nization technique [4, 5, 8, 14, 77], which exploits the information available  
25 at the smallest scale characterizing the considered medium or phenomenon to  
26 obtain an effective description of the medium or phenomenon itself valid at  
27 its largest scale. This is achieved by expanding in asymptotic series the equa-  
28 tions constituting the mathematical model formulated at the lowest scale. As  
29 a result, the coefficients of the effective governing equations encode the infor-  
30 mation on the other hierarchical levels, as they are to be computed solving  
31 microstructural problems at the smaller scales. The multi-scale asymptotic  
32 homogenization approach has been successfully applied to investigate var-  
33 ious physical systems due to its potentiality in decreasing the complexity  
34 of the problem at hand. Biomechanical applications of asymptotic homoge-  
35 nization may be found mainly in nanomedicine [81], biomaterials modeling,  
36 such as the bone [58, 65], tissue engineering [24], poroelasticity [63], and ac-  
37 tive elastomers [64]. Most of the literature concerning applications of the  
38 asymptotic homogenization technique focuses on linearized governing equa-  
39 tions, as in this case it is possible to obtain, under a number of simplifying  
40 assumptions, a full decoupling between scales, which leads to a dramatic re-  
41 duction in the computational complexity, as also noted for example in [64].  
42 In fact, homogenization in nonlinear mechanics is usually tackled via average  
43 field approaches based on representative volume elements or Eshelby-based  
44 techniques (see e.g. [41] for a comparison between the latter and asymp-  
45 totic homogenization), as done for example in [11]. These homogenization  
46 approaches are typically well-suited when seeking for suitable bounds for the  
47 coefficients of the model, such as the elastic moduli, while asymptotic ho-  
48 mogenization can provide a precise characterization of the coefficients under  
49 appropriate regularity assumptions (namely, *local periodicity*).

50 However, to the best of our knowledge and understanding, there exists  
51 only a few examples, e.g. [15, 68, 74, 75], dealing with the asymptotic ho-  
52 mogenization in the case of media undergoing large deformations. In [68],  
53 the static microstructural effects of periodic hyperelastic composites at finite

54 strain are investigated. In [74], the interactions between large deforming solid  
55 and fluid media at the microscopic level are described by using the two-scale  
56 homogenization technique and the updated Lagrangian formulation. In [15],  
57 the effective equations describing the flow, elastic deformation and transport  
58 in an active poroelastic medium were obtained. Therein, the authors consid-  
59 ered the spatial homogenization of a coupled transport and fluid-structure  
60 interaction model, incorporating details of the microscopic system and ad-  
61 mitting finite growth and deformation at the pore scale. Some works can be  
62 also found dealing with homogenization in the case of elastic perfectly plastic  
63 constituents [79, 83].

64 Here we embrace the asymptotic homogenization approach and consider  
65 a heterogeneous body composed of two hyperelastic solid constituents sub-  
66 jected to the evolution of their internal structure. We refer to this phe-  
67 nomenon as to material remodeling and we interpret it with the production  
68 of plastic-like distortions. The wording “material remodeling” is used as a  
69 synonym of “evolution of the internal structure” of a tissue, and is intended in  
70 the sense of [16], who states that “*biological systems can adapt their structure*  
71 *[...] to accommodate a changed mechanical load environment*”. In this case,  
72 always in the terminology of [16] and [80], one speaks of *epigenetic* adap-  
73 tation (or material remodeling). In the framework of the manuscript, such  
74 adaptation is assumed to occur through plastic-like distortions that represent  
75 processes like the redistribution of the adhesion bonds among the tissue cells.

76 It is worth to recall in which sense the concept of “plastic distortions”,  
77 conceived in the context of the Theory of Plasticity (cf. e.g. [50, 55]),  
78 and originally referred to non-living materials such as metals or soils, can  
79 be imported to describe the structural evolution of biological tissues. To  
80 this end, it is important to emphasize that the wording “plastic distortions”  
81 is understood as the result of a complex of transformations that conducts  
82 to the reorganization of the internal structure of a material, and that —  
83 as anticipated in the Introduction— such reorganization is referred to as  
84 “remodeling” in the biomechanical context.

85 The ways in which the structural transformations may take place in a  
86 given material depend on the structural properties of the material itself. For  
87 this reason, the plasticity in metals is markedly different from that occurring  
88 in amorphous materials. In the case of metals, indeed, for which the internal  
89 structure is granular and characterized by the arrangement of the atomic lat-  
90 tice within each grain, plastic distortions are the *macroscopic* manifestation  
91 of the formation and evolution of lattice defects. As reported in [55], such

92 defects can be due, for example, to edge dislocations, wedge disclinations,  
93 missing atoms at some lattice sites, or to the presence of atoms in the lat-  
94 tice interstices. To describe how the defects evolve, thereby giving rise to the  
95 plastic distortions, one should compare the real lattice at the current instant  
96 of time with an ideal lattice, and decompose the overall deformation (i.e.,  
97 shape change *and* structural transformation) into an elastic and an inelastic  
98 contribution [55]. The elastic contribution describes the part of deformation  
99 that is recoverable by completely relaxing mechanical stress, whereas the in-  
100 elastic contribution represents the structural variation, which, in general, is  
101 of irreversible nature.

102 Clearly, metals have structural features markedly different from those of  
103 living matter. Still, some of the fundamental mechanisms that trigger the  
104 reorganization of their internal structure can be adapted to describe the  
105 remodeling of biological tissues.

106 For instance, in the case of bones, plastic-like phenomena are due to  
107 the formation of microcracks that, in turn, favors the gliding of the material  
108 along the direction of the opening of the cracks [17, 86]. Lastly, as anticipated  
109 above, in the case of biological tissues such as cellular aggregates, the phe-  
110 nomenon analogous to the generation of dislocations is the rearrangement of  
111 the adhesion bonds among the cells or the reorganization of the extracellular  
112 matrix due to the reorientation of the collagen fibers or their deposition and  
113 resorption, as is the case for blood vessels [48]. Also in all these situations,  
114 the comparison of the real configuration of the tissue with an “ideal” one,  
115 taken as reference, permits the separation of the overall deformation into an  
116 elastic part and a structure-related, “plastic-like” part.

117 Here, taking inspiration from the theory of finite Elastoplasticity [55, 78,  
118 34], we describe the plastic-like distortions by invoking the Bilby-Kröner-Lee  
119 (BKL) decomposition of the deformation gradient tensor, and rephrasing it in  
120 a scale-dependent fashion. We remark that, at each of the medium’s charac-  
121 teristic scales, a tensor of plastic distortions is introduced, which accounts for  
122 the fact that the structural variations of the medium cannot be expressed, in  
123 general, in terms of compatible deformations. Our study is conducted within  
124 a purely mechanical framework and under the assumption of negligible iner-  
125 tial forces. These hypotheses imply that the model equations reduce to a set  
126 comprising a scale-dependent, quasi-static law of balance of linear momen-  
127 tum and an evolution law for the tensor of plastic-like distortions. The latter  
128 one is assumed to obey a phenomenological flow rule driven by stress.

129 The manuscript is organized as follows. In Section 2, we introduce the

130 fundamental notions related to the separation of scales, kinematics, and the  
 131 Bilby-Kröner-Lee decomposition for the heterogeneous material. Therein,  
 132 the kinematics of the considered medium is discussed, which has to account  
 133 for the different length-scales characterizing the heterogeneities and results  
 134 into the definition of a scale-dependent deformation gradient tensor. In Sec-  
 135 tion 3, the problem to be solved is formulated, and in Section 4, the two-  
 136 scales asymptotic homogenization technique is applied to obtain the local  
 137 and the homogenized sub-problems. In Section 5, we prescribe a constitutive  
 138 equation for the response of the material and, independently, an evolution  
 139 equation for the tensor of plastic-like distortions. In that respect, the local  
 140 and homogenized problems derived in Section 4 are formulated by consid-  
 141 ering the De Saint-Venant strain energy density and we demonstrate the  
 142 relationship between our new model and the classical ones. In Section 6 we  
 143 outline a computational scheme to solve the resulting up-scaled model and,  
 144 in Section 7, we address the numerical results of our simulations. Finally,  
 145 some concluding remarks on the ongoing work, along with suggestions for  
 146 future research, are summarized in Section 8. We highlight the novelty of  
 147 our approach, and we explain how it may contribute to the understanding of  
 148 the mechanics of heterogeneous media with evolving micro-structure.

## 149 2. Theoretical background

### 150 2.1. Separation of scales

151 The homogenization of a highly heterogeneous medium is only possible  
 152 when the characteristic length of the the local structure ( $\ell_0$ ) and the char-  
 153 acteristic length of the material, or of the phenomenon, of interest ( $L_0$ ) are  
 154 well separated. This condition of separation of scales can be expressed as

$$\varepsilon_0 := \frac{\ell_0}{L_0} \ll 1. \quad (1)$$

155 There may exist more than two coexisting scales and, if they are well sepa-  
 156 rated from each other, a homogenization approach is possible. In this case,  
 157 we then move from the smallest scale to the largest one by homogenization  
 158 [1, 8, 51, 82, 69].

159 Condition (1) is taken as a base assumption for all homogenization pro-  
 160 cesses. The two characteristic length scales  $\ell_0$  and  $L_0$  introduce two di-  
 161 mensionless spatial variables in the reference configuration,  $\tilde{Y} = X/\ell_0$  and  
 162  $\tilde{X} = X/L_0$ , where  $X$  is said to be the *physical spatial variable*, whereas  $\tilde{Y}$

163 and  $\tilde{X}$  represent the microscopic and the macroscopic non-dimensional spa-  
 164 tial variables, respectively. By using (1),  $\tilde{Y}$  and  $\tilde{X}$  can be related through  
 165 the expression

$$\tilde{Y} = \varepsilon_0^{-1} \tilde{X}. \quad (2)$$

166 Given a field  $\Phi$  defined over the region of interest of the heterogeneous  
 167 medium, the separation of scales allows to rephrase the space dependence of  
 168  $\Phi$  as  $\Phi(X) = \check{\Phi}(\tilde{X}(X), \tilde{Y}(X))$ , and the spatial derivative of  $\Phi$  takes thus the  
 169 form

$$\text{Grad}_X \Phi = L_0^{-1} (\text{Grad}_{\tilde{X}} \check{\Phi} + \varepsilon_0^{-1} \text{Grad}_{\tilde{Y}} \check{\Phi}). \quad (3)$$

170 By following this approach, all equations should be written in non-dimensional  
 171 form. In the literature, the switch to the auxiliary variables  $\tilde{X}$  and  $\tilde{Y}$  is often  
 172 omitted. However, as shown for example in [4], both paths are equivalent,  
 173 provided that the dimensional formulation of the problem consistently ac-  
 174 counts for any asymptotic behavior of the involved fields and parameters  
 175 (see e.g. [62] and the discussion therein concerning problems where such a  
 176 behavior is actually deduced via a non-dimensional analysis). By exploiting  
 177 this result, in what follows, our analysis is carried out directly in a system of  
 178 physical variables  $X$  and  $Y$ . Moreover, by adopting the approach usually fol-  
 179 lowed in asymptotic multiscale analysis, we assume that each field and each  
 180 material property characterizing the considered medium are functions of both  
 181  $X$  and  $Y$ , with  $Y = \varepsilon_0^{-1} X$ . Roughly speaking, the dependence on  $X$  captures  
 182 the behavior of a given physical quantity over the largest length-scale, while  
 183 the dependence on  $Y$  captures the behavior over the smallest one. We express  
 184 this property by introducing the notation  $\Phi^\varepsilon(X) = \Phi(X, \varepsilon_0^{-1} X) = \Phi(X, Y)$   
 185 [66]. Moreover, for a fixed  $X$ , we assume that  $\Phi(X, Y)$  is periodic with  
 186 respect to  $Y$ .

187 In the classical theory of two-scale asymptotic homogenization [5, 8, 14],  
 188 the small scaling dimensionless parameter  $\varepsilon_0$  is constant. However, in the  
 189 case of a composite material subjected to deformation and change of internal  
 190 structure (as is the case, for instance, when plastic-like distortions occur),  
 191 the characteristic macroscopic and microscopic lengths, which refer to the  
 192 body and to its heterogeneities, respectively, depend on  $X$  and  $t$ , and should  
 193 thus be denoted by  $\ell(X, t)$  and  $L(X, t)$ . Therefore, the corresponding scaling  
 194 parameter, obtained as the ratio  $\varepsilon(X, t) = \ell(X, t)/L(X, t)$ , is also a func-  
 195 tion of  $X$  and  $t$ , which need not be equal to  $\varepsilon_0$  in general. This variability

196 notwithstanding, if  $\varepsilon(X, t)$  is bounded from above for all  $X$  and for all  $t$ ,  
 197 and if the upper bound is much smaller than unity, we can indicate such  
 198 upper bound with  $\varepsilon$ , and use this constant as a scaling parameter for our  
 199 asymptotic analysis.

## 200 2.2. Kinematics

201 Let us denote by  $\mathcal{B}^\varepsilon$  a continuum body with periodic microstructure, and  
 202 by  $\mathcal{S}$  the three-dimensional Euclidean space. Furthermore, we denote by  
 203  $\mathcal{B}_0^\varepsilon$  the reference, unloaded configuration of  $\mathcal{B}^\varepsilon$ , in which the body's periodic  
 204 micro-structure is reproduced. Now, let us assume that  $\chi^\varepsilon : \mathcal{B}_0^\varepsilon \times \mathcal{T} \rightarrow \mathcal{S}$   
 205 describes the motion of the heterogeneous body, where  $\mathcal{T} = [t_0, t_f[$  is an  
 206 interval of time. Then, the region occupied by the body at time  $t \in \mathcal{T}$   
 207 is  $\mathcal{B}_t^\varepsilon := \chi^\varepsilon(\mathcal{B}_0^\varepsilon, t) \subset \mathcal{S}$  and is said to be its current configuration. Each  
 208 point  $x \in \mathcal{B}_t^\varepsilon$  is such that  $x = \chi^\varepsilon(X, t)$ , with  $X \in \mathcal{B}_0^\varepsilon$  being the point's  
 209 reference placement. The deformation from  $\mathcal{B}_0^\varepsilon$  to  $\mathcal{B}_t^\varepsilon$  is characterized by the  
 210 deformation gradient,  $\mathbf{F}^\varepsilon(X, t)$ , which is defined as  $\mathbf{F}^\varepsilon(X, t) = T\chi^\varepsilon(X, t)$   
 211 [53], with  $T\chi^\varepsilon$  being the tangent map of the motion  $\chi^\varepsilon$ , defined from the  
 212 tangent space  $T_X\mathcal{B}_0^\varepsilon$  into  $T_x\mathcal{S}$ . In the sequel, however, since our focus is on  
 213 Homogenization Theory, we find it convenient to use the less formal definition

$$\mathbf{F}^\varepsilon = \mathbf{I} + \text{Grad}\mathbf{u}^\varepsilon, \quad (4)$$

214 where  $\mathbf{I}$  is the second-order identity tensor and  $\text{Grad}\mathbf{u}^\varepsilon$  denotes the gradient  
 215 operator of the displacement  $\mathbf{u}^\varepsilon$ . The condition  $J^\varepsilon = \det\mathbf{F}^\varepsilon > 0$  must be  
 216 satisfied in order for  $\chi^\varepsilon$  to be admissible. The symmetric, positive definite,  
 217 second-order tensor  $\mathbf{C}^\varepsilon = (\mathbf{F}^\varepsilon)^T\mathbf{F}^\varepsilon$  is the right Cauchy-Green deformation  
 218 tensor induced by  $\mathbf{F}^\varepsilon$ . For our purposes, we partition  $\mathcal{B}_0^\varepsilon$  into two sub-  
 219 domains  $\mathcal{B}_0^1$  and  $\mathcal{B}_0^2$ , such that  $\bar{\mathcal{B}}_0^1 \cup \bar{\mathcal{B}}_0^2 = \bar{\mathcal{B}}_0^\varepsilon$  and  $\bar{\mathcal{B}}_0^1 \cap \bar{\mathcal{B}}_0^2 = \mathcal{B}_0^1 \cap \bar{\mathcal{B}}_0^2 = \emptyset$ ,  
 220 where the bar over a set denotes its closure. We let  $\Gamma_0^\varepsilon$  stand for the interface  
 221 between  $\mathcal{B}_0^1$  and  $\mathcal{B}_0^2$ . Particularly,  $\mathcal{B}_0^1$  denotes the matrix of  $\mathcal{B}^\varepsilon$  (also referred  
 222 to as *host phase*) and  $\mathcal{B}_0^2$  a collection of  $N$  disjoint inclusions. The periodic  
 223 cell in the reference configuration is denoted by  $\mathcal{Y}_0$ . The portion of matrix  
 224 contained in  $\mathcal{Y}_0$  is indicated by  $\mathcal{Y}_0^1$ , while  $\mathcal{Y}_0^2$  is the inclusion in  $\mathcal{Y}_0$ . In each  
 225 cell,  $\mathcal{Y}_0^1$  and  $\mathcal{Y}_0^2$  are such that  $\bar{\mathcal{Y}}_0^1 \cup \bar{\mathcal{Y}}_0^2 = \bar{\mathcal{Y}}_0$  and  $\bar{\mathcal{Y}}_0^1 \cap \bar{\mathcal{Y}}_0^2 = \mathcal{Y}_0^1 \cap \bar{\mathcal{Y}}_0^2 = \emptyset$ . The  
 226 symbol  $\Gamma_0$  indicates the interface between  $\mathcal{Y}_0^1$  and  $\mathcal{Y}_0^2$ . In the present work, we  
 227 assume that the periodicity of the body's micro-structure is preserved even  
 228 though the body evolves by both changing its shape and varying its internal  
 229 structure. In general, however, this is not the case. Clearly, our hypothesis is



230 unrealistic in several circumstances, but it might be helpful to describe those  
 231 situations in which the breaking of the material symmetries occurs at a scale  
 232 different from those of interest, as is the case, for instance, when the plastic  
 233 distortions occur in a tissue with evolving material properties [49], that are  
 234 not directly related to the change of the tissue's micro-geometry. On the  
 235 other hand, for nonperiodic media, the macro model is still valid when one  
 236 assumes local boundedness. In that case, the coefficients are simply to be  
 237 retrieved experimentally, as the “cell” problem is no longer to be computed  
 238 on the cell but on the whole micro domain, which would be more complex  
 239 than the original problem.

240 Moreover, we define  $\chi_1^\varepsilon := \chi^\varepsilon|_{\mathcal{B}_0^1} : \mathcal{B}_0^1 \times \mathcal{T} \rightarrow \mathcal{S}$  such that  $\mathcal{B}_t^1 := \chi_1^\varepsilon(\mathcal{B}_0^1, t)$   
 241 denotes the host phase at the current configuration and  $\chi_2^\varepsilon := \chi^\varepsilon|_{\mathcal{B}_0^2} : \mathcal{B}_0^2 \times$   
 242  $\mathcal{T} \rightarrow \mathcal{S}$ , with  $\mathcal{B}_t^2 := \chi_2^\varepsilon(\mathcal{B}_0^2, t)$  denoting the inclusions. Specifically, we enforce  
 243 the condition  $\bar{\mathcal{B}}_t^1 \cup \bar{\mathcal{B}}_t^2 = \bar{\mathcal{B}}_t^\varepsilon$ , with  $\bar{\mathcal{B}}_t^1 \cap \bar{\mathcal{B}}_t^2 = \mathcal{B}_t^1 \cap \bar{\mathcal{B}}_t^2 = \emptyset$ , and denote by  $\Gamma_t^\varepsilon$  the  
 244 interface between  $\mathcal{B}_t^1$  and  $\mathcal{B}_t^2$ . In addition, we let  $\mathcal{Y}_t$  indicate the periodic cell  
 245 in the current configuration, with  $\bar{\mathcal{Y}}_t^1 \cup \bar{\mathcal{Y}}_t^2 = \bar{\mathcal{Y}}_t$ ,  $\bar{\mathcal{Y}}_t^1 \cap \mathcal{Y}_t^2 = \mathcal{Y}_t^1 \cap \bar{\mathcal{Y}}_t^2 = \emptyset$ , and  
 246 with  $\Gamma_t$  being the interface between  $\mathcal{Y}_t^1$  and  $\mathcal{Y}_t^2$  (see Fig. 1). We emphasize  
 247 that  $\mathcal{Y}_t^1$  is the portion of matrix and  $\mathcal{Y}_t^2$  is the inclusion in  $\mathcal{Y}_t$ . We note that  
 248 inside a single cell it can be present also a collection of inclusions and, in  
 249 such a case, we should consider multiple interface conditions [60].

### 250 2.3. Multiplicative decomposition

251 When the body  $\mathcal{B}^\varepsilon$  is subjected to a system of external loads, the change  
 252 of its shape could be accompanied by a rearrangement of its intrinsic struc-  
 253 ture. This process is generally inelastic and may not be described just in  
 254 terms of deformation. Moreover, when mechanical agencies are removed, the  
 255 body is generally unable to recover the unloaded configuration  $\mathcal{B}_0^\varepsilon$ , and may  
 256 occupy a configuration characterized by the presence of residual stresses and  
 257 strains. To bring the body into a fully relaxed state, an ideal tearing process  
 258 has to be introduced [55]. More specifically, for each material point  $X \in \mathcal{B}^\varepsilon$ ,  
 259 we individuate a small neighborhood of  $X$ , referred to as *body element*, we  
 260 ideally cut it out from the body, and we let it relax until it reaches a stress-  
 261 free state. Such state is the *ground state* of the relaxed body element and  
 262 is called *natural state*. This concept, originally used in the theory of elasto-  
 263 plasticity (see [50, 55]), has been used in the biomechanical context by various  
 264 authors like, for instance, [23, 76, 30, 26, 27, 42, 44, 18, 55, 34, 19]. Before  
 265 going further with the use of the BKL decomposition, we mention that, in  
 266 the literature, there exist other approaches to the issue of residual stresses in

267 biological tissues, which call neither for the multiplicative decomposition of  
 268 the deformation gradient tensor, nor for the introduction of an “intermediate,  
 269 relaxed configuration”. One recent publication adhering to this philosophy  
 270 is for example [13], in which the authors warn that the intermediate config-  
 271 uration may “*not exist in physical reality and must be postulated a priori*”.  
 272 Although we are aware of the fact that a framework based on the BKL-  
 273 decomposition may lead in some cases to assume unrealistic results —as any  
 274 other framework would do—, we prefer here to adhere to the BKL approach  
 275 for consistency with previous works of ours.

276 By performing the ideal process described above for all the body points, a  
 277 collection of relaxed body pieces is obtained, in which each piece finds itself  
 278 in its natural state. We denote such collection by  $\mathcal{B}_\nu^\varepsilon$ . In the language of  
 279 continuum mechanics, these physical considerations lead to the BKL decom-  
 280 position [55, 34]. Although summarizing these theoretical results is useful for  
 281 sake of completeness, the consequences of the BKL decomposition are well-  
 282 known, as it is one the pillars of Elastoplasticity. For this reason, we do not  
 283 fuss over its theoretical justification, and we highlight, rather, the fact that  
 284 one of the purposes of this work is to investigate the use of a scale-dependent  
 285 BKL decomposition. In detail, by referring to Figure 1, we invoke a multi-  
 286 plicative decomposition of the deformation gradient  $\mathbf{F}^\varepsilon$  that is parameterized  
 287 by the scaling ratio  $\varepsilon$ , i.e.,

$$\mathbf{F}^\varepsilon = \mathbf{F}_e^\varepsilon \mathbf{F}_p^\varepsilon, \quad (5)$$

288 where the tensors  $\mathbf{F}_e^\varepsilon$  and  $\mathbf{F}_p^\varepsilon$  describe, respectively, the elastic and the in-  
 289 elastic distortions contributing to  $\mathbf{F}^\varepsilon$ . Along with (5), we also define the  
 290 determinants  $J_e^\varepsilon = \det(\mathbf{F}_e^\varepsilon)$  and  $J_p^\varepsilon = \det(\mathbf{F}_p^\varepsilon)$ , which are both strictly posi-  
 291 tive. Consistently with the notation introduced above, it holds true that  
 292  $\mathbf{F}_e^\varepsilon(X) = \mathbf{F}_e(X, Y)$ ,  $\mathbf{F}_p^\varepsilon(X) = \mathbf{F}_p(X, Y)$ , and  $\mathbf{F}^\varepsilon(X) = \mathbf{F}(X, Y)$  as well as  
 293  $J_e^\varepsilon(X) = J_e(X, Y)$  and  $J_p^\varepsilon(X) = J_p(X, Y)$ .

294 In this work, we focus on remodeling, i.e., plastic-like distortions that  
 295 occur to modify the internal structure of  $\mathcal{B}^\varepsilon$ . Although this phenomenon is  
 296 not visible, it could lead to the alteration of the mechanical properties of  $\mathcal{B}^\varepsilon$ .

### 297 3. Formulation of the problem

298 We consider a composite material comprising two solid constituents, whose  
 299 point-wise constitutive response is hyperelastic. Therefore, to model its me-  
 300 chanical behavior, we introduce the scale-dependent strain energy function,

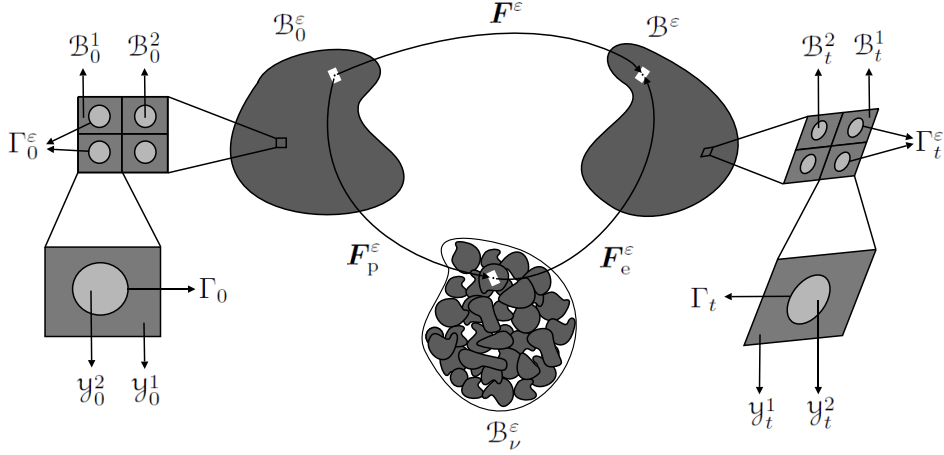


Figure 1: Schematic of a composite material with periodic internal micro-structure and subjected to inelastic remodeling distortions. From left to right: Magnification of an excerpt of material and description of its nested, periodic micro-structure. Change of shape of the body from the reference to the current configuration, and definition of the conglomerate of relaxed body pieces, each in its natural state. Magnification of an excerpt of material, taken from the body's current configuration, and description of its deformed, and remodeled, micro-structure.

301 defined per unit volume of the natural state,

$$\check{\psi}_\nu(X, t) = \psi_\nu^\epsilon(\mathbf{F}_e^\epsilon(X, t), i^\epsilon(X, t)) = \psi_\nu(\mathbf{F}_e(X, Y, t), i(X, Y, t)), \quad (6)$$

302 where  $i$  is defined by the expression  $i(X, Y, t) = (X, Y)$ , i.e.,  $i$  extracts the  
 303 spatial pair  $(X, Y)$  from the triplet  $(X, Y, t)$ . From (6) we can derive the first  
 304 Piola-Kirchhoff stress tensor,

$$\mathbf{T}^\epsilon = J_p^\epsilon \frac{\partial \psi_\nu^\epsilon}{\partial \mathbf{F}_e^\epsilon} (\mathbf{F}_p^\epsilon)^{-T}, \quad (7)$$

305 where  $J_p^\epsilon = \det \mathbf{F}_p^\epsilon$ . In particular, if we neglect body forces and inertial terms,  
 306 the balance of linear momentum reads,

$$\begin{cases} \text{Div } \mathbf{T}^\epsilon = \mathbf{0}, & \text{in } \mathcal{B}_0^\epsilon \setminus \Gamma_0^\epsilon \times \mathcal{T}, \\ \mathbf{T}^\epsilon \cdot \mathbf{N} = \bar{\mathbf{T}}, & \text{on } \partial_T \mathcal{B}_0^\epsilon \times \mathcal{T}, \\ \mathbf{u}^\epsilon = \bar{\mathbf{u}}, & \text{on } \partial_u \mathcal{B}_0^\epsilon \times \mathcal{T}, \end{cases} \quad (8)$$

307 where  $\bar{\mathbf{T}}$  and  $\bar{\mathbf{u}}$  are, respectively, the prescribed traction and displacement  
 308 on the boundary  $\partial \mathcal{B}_0^\epsilon = \partial_T \mathcal{B}_0^\epsilon \cup \partial_u \mathcal{B}_0^\epsilon$  with  $\bar{\partial}_T \mathcal{B}_0^\epsilon \cap \partial_u \mathcal{B}_0^\epsilon = \partial_T \mathcal{B}_0^\epsilon \cap \bar{\partial}_u \mathcal{B}_0^\epsilon = \emptyset$

309 and  $\mathbf{N}$  is the outward unit vector normal to the surface  $\partial\mathcal{B}_0^\varepsilon$ . Continuity  
 310 conditions for displacement and traction are imposed,

$$[[\mathbf{u}^\varepsilon]] = \mathbf{0} \quad \text{and} \quad [[\mathbf{T}^\varepsilon \cdot \mathbf{N}_y]] = \mathbf{0}, \quad \text{on } \Gamma_0 \times \mathcal{T}, \quad (9)$$

311 where  $[[\bullet]]$  denotes the jump across the interface between the two constituents  
 312 and  $\mathbf{N}_y$  defines the unit outward normal to  $\Gamma_0$ . Moreover, problem (8)  
 313 must be supplemented with an appropriate evolution law for  $\mathbf{F}_p^\varepsilon$ . It is worth  
 314 mentioning that the homogenization process can be performed regardless of  
 315 the particular choice of *external* boundary conditions (Dirichlet-Neumann  
 316 in this case). This means that the formulation presented in this work is  
 317 potentially applicable also to other external boundary conditions, such as  
 318 e.g. those of Robin-type. This is due to the fact that, as pointed out in [69],  
 319 also in the present study the homogenization is applied in regions sufficiently  
 320 far away from the outer boundary of the considered medium. For problems  
 321 in which it is necessary to homogenize also close to the outer heterogeneous  
 322 boundaries, we refer to [8, 57, 46].

323 **Remark 1.** *In the present work, we impose conditions (9) for displacements*  
 324 *and tractions just to exemplify the homogenization technique applied to het-*  
 325 *erogeneous media with evolving microstructure. In other words, we assume*  
 326 *that the contact interface between the constituents is ideal. This means that*  
 327 *the displacements are congruent, and thus continuous, and that linear mo-*  
 328 *mentum is conserved across the interface, which in our context implies the*  
 329 *continuity of the tractions. However, the hypothesis of the ideal interface can*  
 330 *be relaxed in some biological situations. For instance, in cancerous tissues,*  
 331 *there exist cross-links between normal and malignant cells, whose density and*  
 332 *strength determine a spring constant that relates the normal stresses on each*  
 333 *cell surface, thereby making it non-ideal [47, 37]. Another example of non-*  
 334 *ideal interface is the periodontal ligament, which represents the thin layer*  
 335 *between the cementum of the tooth to the adjacent alveolar bone [28]. In the*  
 336 *context of composite materials, when non-ideal interfaces are accounted for,*  
 337 *the interface conditions are suitably reformulated [38, 39, 7, 6]. In particular,*  
 338 *the asymptotic homogenization technique has been applied for linear elastic*  
 339 *periodic fiber reinforced composites with imperfect contact between matrix and*  
 340 *fibers (see e.g. [36]).*

341 **4. Asymptotic homogenization of the balance of linear momentum**

342 A formal two-scale asymptotic expansion is performed for the displace-  
 343 ment  $\mathbf{u}^\varepsilon$ , which thus reads

$$\mathbf{u}^\varepsilon(X, t) = \mathbf{u}^{(0)}(X, t) + \sum_{k=1}^{+\infty} \mathbf{u}^{(k)}(X, Y, t) \varepsilon^k, \quad (10)$$

344 where, for all  $k \geq 1$ ,  $\mathbf{u}^{(k)}$  is periodic with respect to  $Y$ . Following [68] we  
 345 consider the leading order term of the expansion (10) to be independent  
 346 of the fast variable  $Y$ . From formula (4), the expansion (10), and taking  
 347 into account the property of scale separation, it follows that the deformation  
 348 gradient tensor can be written as

$$\mathbf{F}^\varepsilon(X, t) = \sum_{k=0}^{+\infty} \mathbf{F}^{(k)}(X, Y, t) \varepsilon^k, \quad (11)$$

349 with the notation

$$\mathbf{F}^{(0)} := \mathbf{I} + \text{Grad}_X \mathbf{u}^{(0)} + \text{Grad}_Y \mathbf{u}^{(1)}, \quad (12a)$$

$$\mathbf{F}^{(k)} := \text{Grad}_X \mathbf{u}^{(k)} + \text{Grad}_Y \mathbf{u}^{(k+1)}, \quad \forall k \geq 1, \quad (12b)$$

350 where  $\text{Grad}_X$  and  $\text{Grad}_Y$  are the gradient operators with respect to  $X$  and  $Y$ ,  
 351 respectively. Now, the following two-scale asymptotic expansion is proposed  
 352 for the first Piola-Kirchhoff stress tensor  $\mathbf{T}^\varepsilon$ ,

$$\mathbf{T}^\varepsilon(X, t) = \sum_{k=0}^{+\infty} \mathbf{T}^{(k)}(X, Y, t) \varepsilon^k, \quad (13)$$

353 where the fields  $\mathbf{T}^{(k)}$  are periodic with respect to  $Y$ . By substituting the  
 354 power series representation (13) into (8), using the scale separation condition,  
 355 and multiplying the result by  $\varepsilon$ , the following multi-scale system is obtained

$$\text{Div} \mathbf{T}^\varepsilon = \sum_{k=0}^{+\infty} \mathfrak{D}^{(k)} \varepsilon^k = \mathbf{0}, \quad (14)$$

356 with

$$\mathfrak{D}^{(0)} := \text{Div}_Y \mathbf{T}^{(0)}, \quad (15a)$$

$$\mathfrak{D}^{(k)} := \text{Div}_X \mathbf{T}^{(k-1)} + \text{Div}_Y \mathbf{T}^{(k)}, \quad \forall k \geq 1. \quad (15b)$$

357 We require that the equilibrium equation (14) is satisfied at every  $\varepsilon$ , which  
 358 amounts to impose the conditions

$$\text{Div}_Y \mathbf{T}^{(0)} = \mathbf{0}, \quad (16a)$$

$$\text{Div}_X \mathbf{T}^{(k-1)} + \text{Div}_Y \mathbf{T}^{(k)} = \mathbf{0}, \quad \forall k \geq 1. \quad (16b)$$

359 At this point we introduce the average operator over the microscopic cell, i.e.

$$\langle \bullet \rangle = \frac{1}{|\mathcal{Y}_t|} \int_{\mathcal{Y}_t} \bullet \, dY, \quad (17)$$

360 where  $|\mathcal{Y}_t|$  represents the volume of the periodic cell  $\mathcal{Y}_t$  at time  $t$ . Indeed,  
 361 because of the deformations and distortions to which the microscopic, refer-  
 362 ence periodic cell is subjected,  $\mathcal{Y}_t$  is different at every time instant. Averaging  
 363 (16b) over the microscopic cell yields, for  $k = 1$ ,

$$\langle \text{Div}_X \mathbf{T}^{(0)} \rangle + \frac{1}{|\mathcal{Y}_t|} \int_{\partial \mathcal{Y}_t} \mathbf{T}^{(1)} \cdot \mathbf{N} \, dY = \mathbf{0}, \quad (18)$$

364 where, on the left-hand side, we have applied the divergence theorem. Since  
 365 the contributions on the periodic cell boundary  $\partial \mathcal{Y}_t$  cancel due to the  $Y$ -  
 366 periodicity, the integral over  $\mathcal{Y}_t$  is equal to zero, and (18) becomes

$$\langle \text{Div}_X \mathbf{T}^{(0)} \rangle = \mathbf{0}. \quad (19)$$

367 Here, we restrict our analysis to the particular case in which the periodic  
 368 cell can be uniquely chosen independently of  $X$ , which implies that the in-  
 369 tegration over  $\mathcal{Y}_t$  and the computation of the divergence commute. This  
 370 assumption is also referred to as *macroscopic uniformity*, see also [9, 40, 59]  
 371 for examples dealing with non-macroscopically uniform media in the context  
 372 of poroelasticity and diffusion. Therefore, Equation (19) can be recast as

$$\text{Div}_X \langle \mathbf{T}^{(0)} \rangle = \mathbf{0}. \quad (20)$$

373 Equations (16a) and (20) represent, respectively, the local and the homoge-  
 374 nized equation associated with the original one, stated in (8). Both equations  
 375 still need to be supplemented with the corresponding interface, boundary, and

376 initial conditions. Note that, although both problems feature no time deriva-  
 377 tive, initial conditions are required because  $\mathbf{T}^{(0)}$  depends on the variable  $\mathbf{F}_p^{(0)}$ ,  
 378 which satisfies an evolution equation in time.

379 We remark that the leading term  $\mathbf{T}^{(0)} = \mathbf{T}^{(0)}(X, Y, t)$  of the multi-scale  
 380 expansion (13) is the unknown, both in (16a) and in (20). To identify  $\mathbf{T}^{(0)}$ ,  
 381 we propose here to expand  $\mathbf{F}_p^\varepsilon$  and  $\psi_\nu^\varepsilon$  as

$$\mathbf{F}_p^\varepsilon(X, t) = \sum_{k=0}^{+\infty} \mathbf{F}_p^{(k)}(X, Y, t) \varepsilon^k, \quad (21a)$$

$$\psi_\nu^\varepsilon(X, t) = \sum_{k=0}^{+\infty} \psi_\nu^{(k)}(\mathbf{F}_e(X, Y, t), X, Y) \varepsilon^k, \quad (21b)$$

382 where  $\mathbf{F}_p^{(k)}$  and  $\psi_\nu^{(k)}$  are periodic in  $Y$ . By using (5), (11) and (21a), we can  
 383 deduce a series expansion for  $\mathbf{F}_e^\varepsilon$  in powers of  $\varepsilon$ , where the leading order term  
 384  $\mathbf{F}_e^{(0)}$  is given by

$$\mathbf{F}_e^{(0)} = \mathbf{F}^{(0)}(\mathbf{F}_p^{(0)})^{-1}. \quad (22)$$

385 Following [15] and [68],  $\mathbf{T}^{(0)}$  is therefore supplied constitutively as

$$\mathbf{T}^{(0)} = J_p^{(0)} \frac{\partial \psi_\nu^{(0)}}{\partial \mathbf{F}_e^{(0)}} (\mathbf{F}_p^{(0)})^{-T}, \quad (23)$$

386 with  $\psi_\nu^{(0)} = \psi_\nu^{(0)}(\mathbf{F}_e^{(0)}(X, Y, t), X, Y)$  and  $J_p^{(0)} = \det \mathbf{F}_p^{(0)}$ . To obtain the  
 387 *cell problem*, equation (14) must be supplemented with the corresponding  
 388 interface conditions. This is done by substituting the asymptotic expansions  
 389 of  $\mathbf{u}^\varepsilon$  and of  $\mathbf{T}^\varepsilon$  into the interface conditions  $[[\mathbf{u}^\varepsilon]] = \mathbf{0}$  and  $[[\mathbf{T}^\varepsilon \cdot \mathbf{N}_y]] = \mathbf{0}$ .  
 390 Both conditions are satisfied at any order of  $\varepsilon$ . At the order  $\varepsilon^0$ , we simply  
 391 obtain  $[[\mathbf{T}^{(0)} \cdot \mathbf{N}_y]] = \mathbf{0}$  for the stresses, and that the condition  $[[\mathbf{u}^{(0)}]] = \mathbf{0}$  is  
 392 trivially satisfied, because  $\mathbf{u}^{(0)}$  depends solely on  $X$  and  $t$ . Thus, the interface  
 393 condition on the displacements is written only for  $\mathbf{u}^{(1)}$  and reads,  $[[\mathbf{u}^{(1)}]] = \mathbf{0}$ .  
 394 By summarizing these results, the cell problem at zero order of the epsilon  
 395 parameter can be stated as

$$\begin{cases} \operatorname{Div}_Y \mathbf{T}^{(0)} = \mathbf{0}, & \text{in } \mathcal{Y}_0 \setminus \Gamma_0 \times \mathcal{T}, \\ [[\mathbf{u}^{(1)}]] = \mathbf{0}, & \text{on } \Gamma_0 \times \mathcal{T}, \\ [[\mathbf{T}^{(0)} \cdot \mathbf{N}_y]] = \mathbf{0}, & \text{on } \Gamma_0 \times \mathcal{T}. \end{cases} \quad (24)$$

396 Together with the cell problem, we also need to formulate the macro-scopic  
 397 homogenized problem. To this end, we take equation (20) and complete it  
 398 with a set of boundary conditions. This is done by substituting the asymp-  
 399 totic expansions of  $\mathbf{T}^\varepsilon$  and  $\mathbf{u}^\varepsilon$  into the boundary conditions  $\mathbf{T}^\varepsilon \cdot \mathbf{N} = \bar{\mathbf{T}}$   
 400 and  $\mathbf{u}^\varepsilon = \bar{\mathbf{u}}$ , respectively. Thus, equating the coefficients at order  $\varepsilon^0$ , and  
 401 averaging the results over the unit cell, we find the *homogenized problem*,

$$\begin{cases} \operatorname{Div}_X \langle \mathbf{T}^{(0)} \rangle = \mathbf{0}, & \text{in } \mathcal{B}_h \times \mathcal{T}, \\ \langle \mathbf{T}^{(0)} \rangle \cdot \mathbf{N} = \bar{\mathbf{T}}, & \text{on } \partial_T \mathcal{B}_h \times \mathcal{T}, \\ \mathbf{u}^{(0)} = \bar{\mathbf{u}}, & \text{on } \partial_u \mathcal{B}_h \times \mathcal{T}, \end{cases} \quad (25)$$

402 where  $\mathcal{B}_h$  denotes the homogeneous macro-scale domain in which the homog-  
 403 enized equations are defined.

404 The problem (25) has to be solved along with a homogenized evolution  
 405 equation for  $\mathbf{F}_p^{(0)}$  and the initial condition associated with it. In addition, we  
 406 remark that, according to (25), the boundary tractions acting on  $\partial_T \mathcal{B}_h$  are  
 407 balanced *only* by the normal component of the average of the leading order  
 408 stress,  $\mathbf{T}^{(0)}$ , and *only* the leading order displacement,  $\mathbf{u}^{(0)}$ , has to be equal  
 409 to the displacement  $\bar{\mathbf{u}}$ , imposed on  $\partial_u \mathcal{B}_h$ .

410 **Remark 2.** *In the medical scientific literature, there exist studies that iden-*  
 411 *tify the existence of anatomical boundary layers interposed between the brain*  
 412 *surface and tumors (see e.g. [72]). Here we do not address boundary layer*  
 413 *phenomena, which are usually neglected in the asymptotic homogenization*  
 414 *literature. The homogenization process described in this work is fine for re-*  
 415 *gions far enough away from the boundary so that its effect is not felt because,*  
 416 *close to the boundaries, the material will not behave as an effective material*  
 417 *with homogenized coefficients. To properly account for boundary effects, the*  
 418 *so-called boundary-layer technique could be used [8, 57].*

## 419 5. Constitutive framework and evolution law

420 In this section, we prescribe a constitutive equation for the response of the  
 421 material and, independently, an evolution equation for the tensor of plastic-  
 422 like distortions.

### 423 5.1. Constitutive law

424 In the following, we formulate the local and homogenized problems for a  
 425 specific constitutive law. In general, this process can be rather cumbersome



426 for complicated strain energy densities, and it becomes even more involved  
 427 when plastic-like distortions are accounted for. To reduce complexity, we  
 428 choose a very simple constitutive law for  $\psi_\nu^\varepsilon$ , such as the De Saint-Venant  
 429 strain energy density,

$$\psi_\nu^\varepsilon = \frac{1}{2} \mathbf{E}_e^\varepsilon : \mathcal{C}^\varepsilon : \mathbf{E}_e^\varepsilon, \quad (26)$$

430 where  $\mathbf{E}_e^\varepsilon = \frac{1}{2} ((\mathbf{F}_e^\varepsilon)^T \mathbf{F}_e^\varepsilon - \mathbf{I})$  is the elastic Green-Lagrange strain tensor and  
 431  $\mathcal{C}^\varepsilon(X) = \mathcal{C}(X, Y)$  is the positive definite fourth-order elasticity tensor, which  
 432 satisfies both major and minor symmetries, i.e.  $\mathcal{C}_{ijkl} = \mathcal{C}_{jikl} = \mathcal{C}_{ijlk} = \mathcal{C}_{klij}$ .  
 433 Particularly, we consider that the constituents of the heterogeneous material  
 434 are isotropic, and thus

$$\mathcal{C}^\varepsilon = 3\kappa^\varepsilon \mathcal{K} + 2\mu^\varepsilon \mathcal{M}, \quad (27)$$

435 where  $\kappa^\varepsilon(X) = \kappa(X, Y)$  is the bulk modulus,  $\mu^\varepsilon(X) = \mu(X, Y)$  is the shear  
 436 modulus, and the fourth-order tensors  $\mathcal{K} = \frac{1}{3}(\mathbf{I} \otimes \mathbf{I})$  and  $\mathcal{M} = \mathcal{I} - \mathcal{K}$   
 437 extract the spherical and the deviatoric part, respectively, of a symmetric  
 438 second-order tensor  $\mathbf{A}$ , i.e.,  $\mathcal{K} : \mathbf{A} = \frac{1}{3} \text{tr}(\mathbf{A}) \mathbf{I}$  and  $\mathcal{M} : \mathbf{A} = \mathbf{A} - \frac{1}{3} \text{tr}(\mathbf{A}) \mathbf{I} :=$   
 439  $\text{dev}(\mathbf{A})$  [84, 85]. We remark that the fourth-order identity tensor  $\mathcal{I}$  is the  
 440 identity operator over the linear subspace of symmetric second-order tensors.  
 441 Indeed, for every  $\mathbf{A}$  such that  $\mathbf{A} = \mathbf{A}^T$ , it holds that  $\mathcal{I} : \mathbf{A} = \mathbf{A}$ . In  
 442 terms of  $\mathbf{I}$ , an explicit expression of  $\mathcal{I}$  is given by  $\mathcal{I} = \frac{1}{2} [\mathbf{I} \otimes \mathbf{I} + \mathbf{I} \overline{\otimes} \mathbf{I}]$  (in  
 443 components:  $\mathcal{I}_{ijkl} = \frac{1}{2} [I_{ik} I_{jl} + I_{il} I_{jk}]$  [17]).

444 We can identify the leading order term in the expansion of the constitutive  
 445 law (26), which reads

$$\psi_\nu^{(0)} = \frac{1}{2} \mathbf{E}_e^{(0)} : \mathcal{C} : \mathbf{E}_e^{(0)}, \quad (28)$$

446 with  $\mathbf{E}_e^{(0)} = \frac{1}{2} ((\mathbf{F}_e^{(0)})^T \mathbf{F}_e^{(0)} - \mathbf{I})$ . We recall that, although the expression of  
 447  $\psi_\nu^{(0)}$  in (28) depends only on  $\mathbf{E}_e^{(0)}$ , the material coefficient  $\mathcal{C}$  is still a two-  
 448 scale function and should be thus interpreted as  $\mathcal{C}(X, Y)$ . As a consequence,  
 449  $\psi_\nu^{(0)}$  is not homogenized yet.

450 By taking into account the major and minor symmetries of  $\mathcal{C}$ , we obtain

$$\mathbf{S}_\nu^{(0)} = \frac{\partial \psi_\nu^{(0)}}{\partial \mathbf{E}_e^{(0)}} = \mathcal{C} : \mathbf{E}_e^{(0)} = \lambda \text{tr}(\mathbf{E}_e^{(0)}) \mathbf{I} + 2\mu \mathbf{E}_e^{(0)}, \quad (29)$$

451 where  $\mathbf{S}_\nu^{(0)}$  is the leading order term of the second Piola-Kirchhoff stress  
 452 tensor written with respect to the natural state,  $\lambda = \kappa - \frac{2}{3}\mu$  is Lamé's  
 453 constant, and  $\mathbf{E}_e^{(0)}$  is given by

$$\mathbf{E}_e^{(0)} = (\mathbf{F}_p^{(0)})^{-T} \left( \mathbf{E}^{(0)} - \mathbf{E}_p^{(0)} \right) (\mathbf{F}_p^{(0)})^{-1}, \quad (30)$$

454 with  $\mathbf{E}^{(0)} = \frac{1}{2} \left( (\mathbf{F}^{(0)})^T \mathbf{F}^{(0)} - \mathbf{I} \right)$  and  $\mathbf{E}_p^{(0)} = \frac{1}{2} \left( (\mathbf{F}_p^{(0)})^T \mathbf{F}_p^{(0)} - \mathbf{I} \right)$ .

455 By pulling  $\mathbf{S}_\nu^{(0)}$  back to the reference configuration, and recalling that the  
 456 plastic-like distortions are assumed to be isochoric in our framework, (i.e.  
 457  $J_p^\varepsilon = 1$ ), we obtain the second Piola-Kirchhoff stress tensor

$$\mathbf{S}^{(0)} = \mathcal{C}_R : (\mathbf{E}^{(0)} - \mathbf{E}_p^{(0)}), \quad (31)$$

458 where

$$\begin{aligned} \mathcal{C}_R &= (\mathbf{F}_p^{(0)})^{-1} \underline{\otimes} (\mathbf{F}_p^{(0)})^{-1} : \mathcal{C} : (\mathbf{F}_p^{(0)})^{-T} \underline{\otimes} (\mathbf{F}_p^{(0)})^{-T} \\ &= 3\lambda \mathcal{K}_p^{(0)} + 2\mu \mathcal{I}_p^{(0)}, \end{aligned} \quad (32)$$

459 is the elasticity tensor pulled-back to the reference configuration through  
 460  $\mathbf{F}_p^{(0)}$ , and, upon setting  $\mathbf{B}_p^{(0)} = (\mathbf{F}_p^{(0)})^{-1} (\mathbf{F}_p^{(0)})^{-T}$ , we employed the notation

$$\mathcal{K}_p^{(0)} = \frac{1}{3} \mathbf{B}_p^{(0)} \otimes \mathbf{B}_p^{(0)}, \quad (33a)$$

$$\mathcal{I}_p^{(0)} = \frac{1}{2} \left[ \mathbf{B}_p^{(0)} \underline{\otimes} \mathbf{B}_p^{(0)} + \mathbf{B}_p^{(0)} \overline{\otimes} \mathbf{B}_p^{(0)} \right]. \quad (33b)$$

461 We remark that  $\mathcal{K}_p^{(0)}$  extracts the “volumetric part” of a generic second-  
 462 order tensor, taken with respect to the inverse plastic metric tensor  $\mathbf{B}_p^{(0)}$  i.e.  
 463 for all  $\mathbf{A} = \mathbf{A}^T$ , it holds that  $\mathcal{K}_p^{(0)} : \mathbf{A} = \frac{1}{3} \text{tr}(\mathbf{B}_p^{(0)} \mathbf{A}) \mathbf{B}_p^{(0)}$ . Furthermore,  
 464  $\mathcal{I}_p^{(0)}$  transforms  $\mathbf{A}$  into  $\mathcal{I}_p^{(0)} : \mathbf{A} = \mathbf{B}_p^{(0)} \mathbf{A} \mathbf{B}_p^{(0)}$  and  $\mathcal{M}_p^{(0)} = \mathcal{I}_p^{(0)} - \mathcal{K}_p^{(0)}$   
 465 extracts the “deviatoric part” of  $\mathbf{A}$  with respect to the metric tensor  $\mathbf{B}_p^{(0)}$ ,  
 466 i.e.  $\mathcal{M}_p^{(0)} : \mathbf{A} = \mathbf{B}_p^{(0)} \mathbf{A} \mathbf{B}_p^{(0)} - \frac{1}{3} \text{tr}(\mathbf{B}_p^{(0)} \mathbf{A}) \mathbf{B}_p^{(0)}$ . We note that similar results  
 467 have been obtained in the case of non-linear elasticity in [25].

468 Next, we notice that  $\mathbf{F}^{(0)}$  can be written as

$$\mathbf{F}^{(0)} = \mathbf{I} + \mathbf{H}, \quad (34)$$

469 with  $\mathbf{H} = \text{Grad}_X \mathbf{u}^{(0)} + \text{Grad}_Y \mathbf{u}^{(1)}$ . Thus, by substituting (34) in  $\mathbf{E}_e^{(0)}$ ,  
 470 the result into (31), and retaining only the terms linear in  $\mathbf{H}$ ,  $\mathbf{S}^{(0)}$  can be  
 471 linearized as

$$\mathbf{S}_{\text{lin}}^{(0)} = \mathcal{C}_R : (\text{sym} \mathbf{H} - \mathbf{E}_p^{(0)}). \quad (35)$$

472 We recall now that, at the leading order, the first Piola-Kirchhoff stress tensor  
 473 reads  $\mathbf{T}^{(0)} = \mathbf{F}^{(0)} \mathbf{S}^{(0)}$ . Hence, its linearized form is given by

$$\mathbf{T}_{\text{lin}}^{(0)} = \mathcal{C}_{\text{R}} : \text{sym} \mathbf{H} - (\mathbf{I} + \mathbf{H})(\mathcal{C}_{\text{R}} : \mathbf{E}_{\text{p}}^{(0)}). \quad (36)$$

474 Looking at the definition of  $\mathcal{C}_{\text{R}}$  in (32), it can be noticed that our model re-  
 475 solves at the macro-scale the structural evolution of the considered medium  
 476 through the dependence of  $\mathcal{C}_{\text{R}}$  on  $\mathbf{F}_{\text{p}}^{(0)}$ , which indeed describes the produc-  
 477 tion of material inhomogeneities [21, 22, 23]. Additionally, our model is also  
 478 capable of simultaneously resolving the material heterogeneities at both the  
 479 micro- and macro-scale through the dependence of  $\mathcal{C}_{\text{R}}$  on  $X$  and  $Y$ . The lat-  
 480 ter dependence in fact, keeps track of the variability of the elastic coefficient  
 481 at both scales.

482 Because of Equations (33a) and (33b),  $\mathcal{C}_{\text{R}}$  possesses the same symmetry  
 483 properties of  $\mathcal{C}$ , i.e.

$$(\mathcal{C}_{\text{R}})_{IJKL} = (\mathcal{C}_{\text{R}})_{JIKL} = (\mathcal{C}_{\text{R}})_{IJLK} = (\mathcal{C}_{\text{R}})_{KLIJ}, \quad (37)$$

484 and therefore,  $\mathbf{T}_{\text{lin}}^{(0)}$  can be written as

$$\mathbf{T}_{\text{lin}}^{(0)} = \mathcal{C}_{\text{R}} : \mathbf{H} - (\mathbf{I} + \mathbf{H})(\mathcal{C}_{\text{R}} : \mathbf{E}_{\text{p}}^{(0)}). \quad (38)$$

485 *Local problem.* Substituting (38) in the equation of the local problem (24),  
 486 the linear momentum balance law is rephrased as

$$\text{Div}_Y [\mathcal{C}_{\text{R}} : \mathbf{H} - (\mathbf{I} + \mathbf{H})(\mathcal{C}_{\text{R}} : \mathbf{E}_{\text{p}}^{(0)})] = \mathbf{0}, \quad (39)$$

487 or, equivalently,

$$\begin{aligned} \text{Div}_Y [\mathcal{C}_{\text{R}} : \text{Grad}_Y \mathbf{u}^{(1)} - \text{Grad}_Y \mathbf{u}^{(1)} (\mathcal{C}_{\text{R}} : \mathbf{E}_{\text{p}}^{(0)})] = \\ - \text{Div}_Y [\mathcal{C}_{\text{R}} : \text{Grad}_X \mathbf{u}^{(0)} - (\mathbf{I} + \text{Grad}_X \mathbf{u}^{(0)}) (\mathcal{C}_{\text{R}} : \mathbf{E}_{\text{p}}^{(0)})]. \end{aligned} \quad (40)$$

488 In the absence of plastic distortions, i.e., when  $\mathbf{F}_{\text{p}}^{\varepsilon} = \mathbf{I}$ , Equation (40) coin-  
 489 cides with the equation of the classical cell problem encountered in the ho-  
 490 mogeneization of linear elasticity, which is known to admit a unique solution,  
 491 up to a  $Y$ -constant function, if the average over the cell of the right-hand-side  
 492 vanishes identically (in the jargon of Homogenization Theory, this condition  
 493 is referred to as *solvability condition* or *compatibility condition*) [5]. In our

494 case, since the pulled-back elasticity tensor  $\mathcal{C}_R$  is periodic in  $Y$ , while  $\mathbf{u}^{(0)}$  is  
 495 independent of  $Y$ , the solvability condition is satisfied, i.e.,

$$\langle \text{Div}_Y [\mathcal{C}_R : \text{Grad}_X \mathbf{u}^{(0)} - (\mathbf{I} + \text{Grad}_X \mathbf{u}^{(0)}) (\mathcal{C}_R : \mathbf{E}_p^{(0)})] \rangle = \mathbf{0}. \quad (41)$$

496 Exploiting the linearity of equation (40) in  $\mathbf{u}^{(1)}$ , we make the *ansatz*

$$\mathbf{u}^{(1)}(X, Y, t) = \boldsymbol{\xi}(X, Y, t) : \text{Grad}_X \mathbf{u}^{(0)}(X, t) + \boldsymbol{\omega}(X, Y, t), \quad (42)$$

497 where  $\boldsymbol{\xi}$  and  $\boldsymbol{\omega}$  are a third-order tensor field and a vector field, both periodic  
 498 in  $Y$ .

499 We now require that  $\boldsymbol{\xi}$  and  $\boldsymbol{\omega}$  satisfy two independent cell problems. The  
 500 cell problem for  $\boldsymbol{\xi}$  reads

$$\left\{ \begin{array}{ll} \text{Div}_Y [\mathcal{C}_R : T\text{Grad}_Y \boldsymbol{\xi} - T\text{Grad}_Y \boldsymbol{\xi} (\mathcal{C}_R : \mathbf{E}_p^{(0)})] \\ \quad = \text{Div}_Y [-\mathcal{C}_R + \mathbf{I} \underline{\otimes} (\mathcal{C}_R : \mathbf{E}_p^{(0)})], & \text{in } \mathcal{Y}_0 \setminus \Gamma_0 \times \mathcal{T}, \\ \llbracket \boldsymbol{\xi} \rrbracket = \mathbf{0}, & \text{on } \Gamma_0 \times \mathcal{T}, \\ \llbracket [\mathcal{C}_R : T\text{Grad}_Y \boldsymbol{\xi} - T\text{Grad}_Y \boldsymbol{\xi} (\mathcal{C}_R : \mathbf{E}_p^{(0)}) \\ \quad + \mathcal{C}_R - \mathbf{I} \underline{\otimes} (\mathcal{C}_R : \mathbf{E}_p^{(0)})] \cdot \mathbf{N}_Y \rrbracket = \mathbf{0}, & \text{on } \Gamma_0 \times \mathcal{T}. \end{array} \right. \quad (43)$$

501 Before going further, some words of explanation on the notation are nec-  
 502 essary. First, we notice that  $\text{Grad}_Y \boldsymbol{\xi}$  is a fourth-order tensor function, which  
 503 admits the representation  $\text{Grad}_Y \boldsymbol{\xi} = (\partial \xi_{ABC}) / (\partial Y_D) \mathbf{e}_A \otimes \mathbf{e}_B \otimes \mathbf{e}_C \otimes \mathbf{e}_D$ . Then,  
 504  $T\text{Grad}_Y \boldsymbol{\xi}$  is a fourth-order tensor function obtained by ordering the indices  
 505 of  $\text{Grad}_Y \boldsymbol{\xi}$  in the following fashion

$$\begin{aligned} T\text{Grad}_Y \boldsymbol{\xi} &= (T\text{Grad}_Y \boldsymbol{\xi})_{ABCD} \mathbf{e}_A \otimes \mathbf{e}_B \otimes \mathbf{e}_C \otimes \mathbf{e}_D \\ &= (\text{Grad}_Y \boldsymbol{\xi})_{ACDB} \mathbf{e}_A \otimes \mathbf{e}_B \otimes \mathbf{e}_C \otimes \mathbf{e}_D \\ &= \frac{\partial \xi_{ACD}}{\partial Y_B} \mathbf{e}_A \otimes \mathbf{e}_B \otimes \mathbf{e}_C \otimes \mathbf{e}_D. \end{aligned} \quad (44)$$

506 The cell problem for  $\boldsymbol{\omega}$  is given by

$$\left\{ \begin{array}{ll} \text{Div}_Y [\mathcal{C}_R : \text{Grad}_Y \boldsymbol{\omega} - \text{Grad}_Y \boldsymbol{\omega} (\mathcal{C}_R : \mathbf{E}_p^{(0)})] \\ \quad = \text{Div}_Y [\mathcal{C}_R : \mathbf{E}_p^{(0)}], & \text{in } \mathcal{Y}_0 \setminus \Gamma_0 \times \mathcal{T}, \\ \llbracket \boldsymbol{\omega} \rrbracket = \mathbf{0}, & \text{on } \Gamma_0 \times \mathcal{T}, \\ \llbracket (\mathcal{C}_R : \text{Grad}_Y \boldsymbol{\omega} - \text{Grad}_Y \boldsymbol{\omega} (\mathcal{C}_R : \mathbf{E}_p^{(0)}) \\ \quad - \mathcal{C}_R : \mathbf{E}_p^{(0)}) \cdot \mathbf{N}_Y \rrbracket = \mathbf{0}, & \text{on } \Gamma_0 \times \mathcal{T}. \end{array} \right. \quad (45)$$

507 By virtue of the linearization process, we obtain two auxiliary cell problems  
508 where the macroscopic term  $\text{Grad}_X \mathbf{u}^{(0)}$  is not explicitly present. Indeed, this  
509 is in general possible only when accounting for the linearized deformations'  
510 regime, see also [15]. Then, the dependence of the macro-scale variable is  
511 given through the tensor  $\mathbf{F}_p^{(0)}$ , which describes the plastic-like distortions.  
512 Moreover, if  $\mathbf{F}_p^{(0)}$  only depends on time, as is the case in [2], the cell problems  
513 are also decoupled in the spatial micro- and macro-variables provided that the  
514 elasticity tensor solely depends on the microscale variable. The cell problems  
515 are in any case time-dependent, as they encode the evolution of the material  
516 response and its link with the plastic-like distortions.

517 *Homogenized problem.* From (36) and (42), the homogenized problem rewrites

$$\begin{cases} \text{Div}_X [\hat{\mathcal{C}}_R : \text{Grad}_X \mathbf{u}^{(0)}] = -\text{Div}_X [\hat{\mathbf{D}}_R], & \text{in } \mathcal{B}_h \times \mathcal{T}, \\ (\hat{\mathcal{C}}_R : \text{Grad}_X \mathbf{u}^{(0)}) \cdot \mathbf{N} + \hat{\mathbf{D}}_R \cdot \mathbf{N} = \bar{\mathbf{T}}, & \text{on } \partial_T \mathcal{B}_h \times \mathcal{T}, \\ \mathbf{u}^{(0)} = \bar{\mathbf{u}}, & \text{on } \partial_u \mathcal{B}_h \times \mathcal{T}, \end{cases} \quad (46)$$

518 where

$$\hat{\mathcal{C}}_R = \langle \mathcal{C}_R + \mathcal{C}_R : T\text{Grad}_Y \boldsymbol{\xi} - T\text{Grad}_Y \boldsymbol{\xi} (\mathcal{C}_R : \mathbf{E}_p^{(0)}) - \mathbf{I} \otimes (\mathcal{C}_R : \mathbf{E}_p^{(0)}) \rangle, \quad (47a)$$

$$\hat{\mathbf{D}}_R = \langle \mathcal{C}_R : \text{Grad}_Y \boldsymbol{\omega} - \text{Grad}_Y \boldsymbol{\omega} (\mathcal{C}_R : \mathbf{E}_p^{(0)}) - \mathcal{C}_R : \mathbf{E}_p^{(0)} \rangle. \quad (47b)$$

519 **Remark 3.** *In the absence of distortions, that is for  $\mathbf{F}_p^\varepsilon = \mathbf{I}$ , the cell prob-*  
520 *lems (43) and (45) reduce to one single cell problem,*

$$\begin{cases} \text{Div}_Y [\mathcal{C} + \mathcal{C} : T\text{Grad}_Y \boldsymbol{\xi}] = \mathbf{0}, & \text{in } \mathcal{Y}_0 \setminus \Gamma_0 \times \mathcal{T}, \\ \llbracket \boldsymbol{\xi} \rrbracket = \mathbf{0}, & \text{on } \Gamma_0 \times \mathcal{T}, \\ \llbracket (\mathcal{C} + \mathcal{C} : T\text{Grad}_Y \boldsymbol{\xi}) \cdot \mathbf{N}_Y \rrbracket = \mathbf{0}, & \text{on } \Gamma_0 \times \mathcal{T}. \end{cases} \quad (48)$$

521 *This is due to the fact that the symmetric tensor  $\mathbf{E}_p^{(0)}$  appearing in (40) is*  
522 *equal to zero. On the other hand, the homogenized problem is rewritten as*  
523 *follows,*

$$\begin{cases} \text{Div}_X [\hat{\mathcal{C}} : \text{Grad}_X \mathbf{u}^{(0)}] = \mathbf{0}, & \text{in } \mathcal{B}_h \times \mathcal{T}, \\ (\hat{\mathcal{C}} : \text{Grad}_X \mathbf{u}^{(0)}) \cdot \mathbf{N} = \bar{\mathbf{T}}, & \text{on } \partial_T \mathcal{B}_h \times \mathcal{T}, \\ \mathbf{u}^{(0)} = \bar{\mathbf{u}}, & \text{on } \partial_u \mathcal{B}_h \times \mathcal{T}, \end{cases} \quad (49)$$

524 where  $\hat{\mathcal{C}} = \langle \mathcal{C} + \mathcal{C} : T\text{Grad}_Y \boldsymbol{\xi} \rangle$  is the effective elasticity tensor. Formula-  
525 tions (48) and (49) are the counterparts of (24) and (25), respectively, when  
526 plastic-like distortions are neglected and a linearized approach for the defor-  
527 mations is considered. Particularly, (48) and (49) identify identically with  
528 classical results in the asymptotic homogenization literature [5, 77].

## 529 5.2. Evolution law

530 Several procedures can be adopted to establish a proper evolution law  
531 for the inelastic distortions. One choice is to follow a phenomenological  
532 approach, which should be based on experimental evidences and comply with  
533 suitable constitutive requirements [29]. On the other hand, one could invoke  
534 some general principles, such as the invariance of the evolution law with  
535 respect to a class of transformations and thermodynamic constraints [21, 22,  
536 23]. Within the latter approach, and adapting the theoretical framework  
537 explored in [21, 22, 23, 29], an evolution equation for the inelastic distortions  
538 has been studied in [19]. Therein, the plastic-like distortions describe a  
539 remodeling process with the following assumptions: (i)  $\mathbf{F}_p$  is restricted by the  
540 constraint  $J_p = 1$ , (ii) the solid phase exhibits hyperelastic behavior, and (iii)  
541 the considered system remodels when the stress induced by external loading  
542 exceeds a characteristic threshold. An evolution law for  $\mathbf{F}_p$  satisfying these  
543 conditions, and compatible with the Dissipation inequality [12, 32, 33, 34],  
544 is given by

$$\text{sym} \left( \mathbf{C} \mathbf{F}_p^{-1} \dot{\mathbf{F}}_p \right) = \gamma \left[ \|\text{dev} \boldsymbol{\sigma}\| - \sqrt{\frac{2}{3}} \sigma_y \right]_+ \frac{\text{dev}(\boldsymbol{\Sigma}) \mathbf{C}}{\|\text{dev} \boldsymbol{\sigma}\|}, \quad (50)$$

545 where  $\boldsymbol{\sigma}$  is the Cauchy stress tensor,  $\text{dev}(\boldsymbol{\Sigma}) = \boldsymbol{\Sigma} - \frac{1}{3} \text{tr}(\boldsymbol{\Sigma}) \mathbf{I}$ , is the deviatoric  
546 part of the Mandell stress tensor  $\boldsymbol{\Sigma} = \mathbf{C} \mathbf{S}$  being the Mandel stress tensor,  
547 and  $\mathbf{S} = \mathbf{F}^{-1} \mathbf{T}$  the second Piola-Kirchhoff stress tensor. Moreover,  $\gamma$  is a  
548 strictly positive model parameter,  $\sigma_y > 0$  is the yield, or threshold, stress,  
549 and the operator  $[A]_+$  is such that, for any real number  $A$ ,  $[A]_+ = A$ , if  $A > 0$ ,  
550 and  $[A]_+ = 0$  otherwise. As anticipated in the Introduction, in the present  
551 context the physical meaning of the plastic-like distortions, represented by  
552  $\mathbf{F}_p$ , is that of structural reorganization, i.e. remodeling, as is the case in  
553 biological tissues when the adhesion bonds among cells or the structure of  
554 the ECM reorganize themselves.

555 Although Equation (50) has been successfully used to describe some bi-  
556 ological situations in which the onset of remodeling is subordinated to the

557 excess of the yield stress  $\sigma_y$ , the homogenization of the evolution law (50) is  
 558 too complicated. For this reason, in this work, we replace (50) with a much  
 559 easier law of the type

$$\text{sym} \left( \mathbf{C}(\mathbf{F}_p)^{-1} \dot{\mathbf{F}}_p \right) = \gamma \text{dev}(\boldsymbol{\Sigma}) \mathbf{C}, \quad (51)$$

560 according to which no stress-activation criterion is supplied. Clearly, this  
 561 choice may turn out to be unrealistic in many circumstances, but it can  
 562 still be useful to understand the essence of some stress-driven remodeling  
 563 processes.

564 We need to clarify that, although in some sentences of this work we  
 565 mentioned growth, our model focuses on *pure* remodeling. This is reflected  
 566 by the condition  $\det \mathbf{F}_p = 1$ , and, more importantly, by the fact that the  
 567 evolution laws (50) and (51) are triggered and controlled exclusively by me-  
 568 chanical factors. On the one hand, the requirement  $\det \mathbf{F}_p = 1$  means that  
 569 the plastic-like distortions are isochoric and, thus, unable to describe volu-  
 570 metric growth. On the other hand, the evolution laws for  $\mathbf{F}_p$ , i.e., Eqs. (50)  
 571 or (51), imply that remodeling is viewed as a consequence of the mechanical  
 572 environment only: When mechanical stress exceeds a given threshold (see  
 573 also [29, 34]), the internal structure of the tissue starts to vary. In other  
 574 words, in the present framework, no biochemical phenomena are accounted  
 575 for as possible activators of remodeling. This is a remarkable difference with  
 576 growth, which, in contrast, occurs only when the concentration of nutrients  
 577 is above a certain threshold value [2, 10, 3, 26, 52]. Our results do not apply  
 578 to growth as they stand, nonetheless, the theory can be adapted to model  
 579 growth by doing some necessary modifications. This is the reason why in  
 580 the abstract we stated that our study offers “*a robust framework that can be*  
 581 *readily generalized to growth and remodeling of nonlinear composites*”.

582 To homogenize (51), the first step is to rewrite it as

$$\text{sym} \left( \mathbf{C}^\varepsilon (\mathbf{F}_p^\varepsilon)^{-1} \dot{\mathbf{F}}_p^\varepsilon \right) = \gamma^\varepsilon \text{dev}(\boldsymbol{\Sigma}^\varepsilon) \mathbf{C}^\varepsilon, \quad (52)$$

583 by admitting that  $\gamma^\varepsilon(X) = \gamma(X, Y)$  is a rapidly oscillating strictly positive  
 584 function. Moreover, by performing the power expansion for  $\boldsymbol{\Sigma}^\varepsilon$ ,

$$\boldsymbol{\Sigma}^\varepsilon(X, t) = \sum_{k=0}^{+\infty} \boldsymbol{\Sigma}^{(k)}(X, Y, t) \varepsilon^k, \quad (53)$$

585 and using (31), the leading order term of  $\Sigma^\varepsilon$  is

$$\Sigma^{(0)} = \mathbf{C}^{(0)}[\mathcal{C}_R : (\mathbf{E}^{(0)} - \mathbf{E}_p^{(0)})]. \quad (54)$$

586 In the limit of small elastic deformations, in (54) we must neglect non-linear  
587 terms in  $\mathbf{H}$ . Therefore,  $\Sigma^{(0)}$  is approximated with

$$\Sigma_{\text{lin}}^{(0)} = \mathcal{C}_R : \text{sym}\mathbf{H} - (\mathbf{I} + 2\text{sym}\mathbf{H})(\mathcal{C}_R : \mathbf{E}_p^{(0)}).$$

588 By virtue of (12a),  $\text{sym}\mathbf{H}$  splits additively as the sum of

$$\text{sym}\mathbf{H} = \mathbf{E}_X^{(0)} + \mathbf{E}_Y^{(1)}, \quad (55)$$

589 where, for  $k = 0, 1$ , and  $j_k = X, Y$ ,

$$\mathbf{E}_{j_k}^{(k)} = \frac{1}{2}[\text{Grad}_{j_k}\mathbf{u}^{(k)} + (\text{Grad}_{j_k}\mathbf{u}^{(k)})^T]. \quad (56)$$

590 By using (55) and (42), we can now rewrite  $\Sigma_{\text{lin}}^{(0)}$  as

$$\Sigma_{\text{lin}}^{(0)} = \mathcal{A}_R : \text{Grad}_X\mathbf{u}^{(0)} + \mathcal{B}_R : \text{Grad}_Y\boldsymbol{\omega} - \mathcal{C}_R : \mathbf{E}_p^{(0)}, \quad (57)$$

591 with

$$\begin{aligned} \mathcal{A}_R &= \mathcal{C}_R + \mathcal{C}_R : T\text{Grad}_Y\xi - \mathbf{I}\underline{\otimes}(\mathcal{C}_R : \mathbf{E}_p^{(0)}) \\ &\quad + [\mathbf{I}\underline{\otimes}(\mathcal{C}_R : \mathbf{E}_p^{(0)})] : [T\text{Grad}_Y\xi + {}^t(T\text{Grad}_Y\xi)], \end{aligned} \quad (58a)$$

$$\mathcal{B}_R = \mathcal{C}_R + \mathbf{I}\underline{\otimes}(\mathcal{C}_R : \mathbf{E}_p^{(0)}). \quad (58b)$$

592 In Equation (58a), the symbol  ${}^t(\bullet)$  transposes the fourth-order tensor to  
593 which it is applied by exchanging the order of its first pair of indices only,  
594 i.e., given an arbitrary fourth-order tensor  $\mathcal{T} = \mathcal{T}_{ABCD}\mathbf{e}_A \otimes \mathbf{e}_B \otimes \mathbf{e}_C \otimes \mathbf{e}_D$ ,  
595  ${}^t\mathcal{T}$  reads

$${}^t\mathcal{T} = \mathcal{T}_{BACD}\mathbf{e}_A \otimes \mathbf{e}_B \otimes \mathbf{e}_C \otimes \mathbf{e}_D. \quad (59)$$

596 Note that in the calculations performed to obtain  $\mathcal{A}_R$  and  $\mathcal{B}_R$  in (57), we  
597 employed the following properties: given two second-order tensors  $\mathbf{A}$  and  $\mathbf{U}$ ,  
598 with  $\mathbf{A}$  being symmetric, it holds that

$$\mathbf{U}\mathbf{A} = (\mathbf{I}\underline{\otimes}\mathbf{A}) : \mathbf{U}, \quad (60a)$$

$$\mathbf{U}^T\mathbf{A} = (\mathbf{I}\overline{\otimes}\mathbf{A}) : \mathbf{U}. \quad (60b)$$



599 Finally, by substituting the expansions of  $\Sigma^\varepsilon$  and  $\mathbf{F}_p^\varepsilon$  in (52), equating  
600 the leading order terms, excluding non-linear terms of  $\mathbf{H}$  and averaging, the  
601 homogenized evolution law for the plastic-like distortions is

$$\text{sym}[\langle \mathbf{C}_{\text{lin}}^{(0)}(\mathbf{F}_p^{(0)})^{-1} \dot{\overline{\mathbf{F}_p^{(0)}}} \rangle] = -\langle \gamma \text{dev}(\Sigma_{\text{lin}}^{(0)}) \rangle - \langle \gamma(\mathcal{C}_R : \mathbf{E}_p^{(0)})(\mathbf{C}_{\text{lin}}^{(0)} - \mathbf{I}) \rangle, \quad (61)$$

602 where  $\Sigma_{\text{lin}}^{(0)}$  is given in (57) and

$$\begin{aligned} \mathbf{C}_{\text{lin}}^{(0)} &= \mathbf{I} + 2\text{sym}\mathbf{H} \\ &= \mathbf{I} + 2(\mathcal{I} + \mathcal{I} : T\text{Grad}_Y \boldsymbol{\xi}) : \text{Grad}_X \mathbf{u}^{(0)} + 2\mathcal{I} : \text{Grad}_Y \boldsymbol{\omega}. \end{aligned} \quad (62)$$

603 We note that, to compute  $\mathbf{C}_{\text{lin}}^{(0)}$ , we must first determine  $\boldsymbol{\xi}$  and  $\boldsymbol{\omega}$ , which is  
604 done by solving the local problems (43) and (45). Furthermore, Equation  
605 (61) needs to be supplemented with an initial condition for  $\mathbf{F}_p^{(0)}$ .

606 **Remark 4.** *In the linearized theory of elasticity, even when the individual*  
607 *constituents of a given composite material are isotropic, the effective elas-*  
608 *tic coefficients may turn out to be anisotropic, depending on the geometric*  
609 *properties of the micro-structure. In fact, when the Homogenization Theory*  
610 *is applied, the anisotropy arises quite naturally due to the solution of the*  
611 *local cell problems [5, 8]. In fact, the homogenized material is anisotropic*  
612 *also in the case of rather simple cells, see for instance [61], where an ex-*  
613 *PLICIT deviation-from-isotropy function is introduced in the context of cubic*  
614 *symmetric elasticity tensors arising from asymptotic homogenization. This*  
615 *has noticeable repercussions also on the evolution law that should be chosen*  
616 *for a correct description of remodeling. To see this, we first notice that, for*  
617 *an isotropic medium, the evolution law of the plastic-like distortions can be*  
618 *formulated in terms of tensor  $\mathbf{B}_p$ , since the constitutive framework is such*  
619 *that  $\mathbf{F}_p$  does not feature explicitly in any constitutive function (see e.g. [78]).*  
620 *In such cases, a possible evolution law for  $\mathbf{B}_p$  may be given in the form*

$$\dot{\mathbf{B}}_p = \gamma \mathbf{B}_p \text{dev}(\Sigma). \quad (63)$$

621 Equation (63) is, in fact, in harmony with the symmetry properties of the  
622 material Mandel stress tensor,  $\Sigma$ , i.e.,  $\mathbf{B}_p \Sigma = (\mathbf{B}_p \Sigma)^T$  [54]. However, if  
623 one writes an equation of the same type as (63) at the scale of a cell problem  
624 (which seems to be a justified choice, because the material is isotropic at  
625 that scale), and then homogenizes, one ends up with a material for which

626 the Mandel stress tensor  $\Sigma$  no longer obeys the symmetry condition  $\mathbf{B}_p \Sigma =$   
627  $(\mathbf{B}_p \Sigma)^T$ . This is because the material is not isotropic at the macroscale  
628 and, thus, the description of remodeling based on  $\mathbf{B}_p$  becomes inadequate.  
629 Therefore, if one wants to homogenize, one should start with evolution laws  
630 at the microscale, which have to be suitable to account for anisotropy, even  
631 though the single constituents are isotropic at that scale. These considerations  
632 lead us to Equation (52), as suggested in [22, 23], and subsequently employed  
633 in [19].

634 **Remark 5.** Equations (50) and (51) can be obtained by adhering to the  
635 philosophy presented in [12, 18], and subsequently adopted, for example, in [3]  
636 for growth, in [44] for growth and remodeling, and in [31, 32] for remodeling  
637 only. Accordingly,  $\mathbf{F}_p$  is regarded as the kinematic descriptor of the structural  
638 degrees of freedom of the medium, and  $\dot{\mathbf{F}}_p$  as the generalized velocity with  
639 which the structural changes occur. Within this setting, it can be proven that  
640 for growth and remodeling problems, the dissipation inequality reads

$$\mathcal{D} = \mathbf{Y}_\nu : \mathbf{L}_p + \mathcal{D}_{\text{nc}} \geq 0, \quad (64)$$

641 where  $\mathcal{D}_{\text{mech}} := \mathbf{Y}_\nu : \mathbf{L}_p$  is the mechanical contribution to dissipation, with  
642  $\mathbf{Y}_\nu$  being the dissipative part of a generalized internal force, dual to  $\mathbf{L}_p$ . In  
643 our work, however,  $\mathbf{Y}_\nu$  can be identified with the tensor  $\mathbf{Y}_\nu \equiv J_p^{-1} \mathbf{F}_p^{-T} \Sigma \mathbf{F}_p^T$ ,  
644 so that  $\mathcal{D}_{\text{mech}}$  coincides with the mechanical dissipation encountered in the  
645 standard formulation of Elastoplasticity, i.e.,  $\mathcal{D}_{\text{mech}} = J_p^{-1} \mathbf{F}_p^{-T} \Sigma \mathbf{F}_p^T : \mathbf{L}_p =$   
646  $J_p^{-1} \Sigma : \mathbf{F}_p^{-1} \dot{\mathbf{F}}_p$ .

647 In the terminology of [45, 30],  $\mathcal{D}_{\text{nc}}$  is referred to as “non-compliant”  
648 contribution to the overall dissipation. Physically, it summarizes a class of  
649 phenomena that are not —or cannot be— resolved in terms of mechanical  
650 power at the scale at which the dissipation inequality is written. For instance,  
651 in the case of growth,  $\mathcal{D}_{\text{nc}}$  may represent biochemical effects contributing to  
652 the overall dissipation.

653 The inequality (64) can be studied in several ways, depending on the prob-  
654 lem at hand. First, we consider a growth problem. To this end, we assume  
655 that  $\mathcal{D}_{\text{nc}}$  can be written as  $\mathcal{D}_{\text{nc}} = r\mathcal{A}$ , where  $r$  is the rate at which mass  
656 is added or depleted from the system (its units are given by the reciprocal  
657 of time), and  $\mathcal{A}$  is the energy density (per unit volume) associated with the  
658 introduction or uptake of mass. In this setting, it is possible to conceive a  
659 particular state of the system in which the mechanical stress is null, i.e.,  
660  $\Sigma = \mathbf{0}$ , while  $r$  and  $\mathcal{A}$  are generally nonzero. When this occurs, the system

661 grows without mechanical dissipation, i.e.,  $\mathcal{D}_{\text{mech}} = 0$ , whereas the overall  
 662 dissipation of the system reduces to the non-compliant one:

$$\mathcal{D} \equiv \mathcal{D}_{\text{nc}} = r\mathcal{A} \geq 0. \quad (65)$$

663 The second case addresses the situation of pure remodeling, for which we  
 664 set  $\mathcal{D}_{\text{nc}} = 0$ , so that the dissipation inequality (64) becomes

$$\mathcal{D} = \mathcal{D}_{\text{mech}} = \mathbf{Y}_\nu : \mathbf{L}_p = J_p^{-1} \boldsymbol{\Sigma} : \mathbf{F}_p^{-1} \dot{\mathbf{F}}_p \geq 0. \quad (66)$$

665 It is possible to show that the evolution laws (50) and (51) are in harmony  
 666 with (66).

## 667 6. A computational scheme for small deformations

668 The macro-scale model given by the problems (46) and (61), together  
 669 with the auxiliary cell problems (43) and (45), requires dedicated numerical  
 670 schemes which are subject of our current investigations. The main compu-  
 671 tational challenge is due to the fact that the local problems depend on the  
 672 macro-scale in a time-dependent way. Therefore, at each time, there is a dif-  
 673 ferent cell problem at each macroscopic point  $X \in \mathcal{B}_h$ . Moreover, one has to  
 674 transfer the information (represented by the geometry, material coefficients,  
 675 and unknowns of the problem) from the cell problems to the homogenized  
 676 problem in the domain  $\mathcal{B}_h$ , and vice versa.

677 Here, as a first step towards the numerical study of this kind of problems,  
 678 we propose an algorithm adapted from [31] that could be useful in our case. In  
 679 [31] it is introduced a computational algorithm, named Generalised Plasticity  
 680 Algorithm (GPA), to study the mechanical response of a biological tissue  
 681 that undergoes large deformations and remodeling of its internal structure.  
 682 Following [31], the discrete and linearized version of the problem constituted  
 683 by Equations (43), (45), (46) and (61) is formulated in three steps.

684 *First step.* The weak form of the cell problems (43) and (45), and of the  
 685 homogenized problem (46) can be *formally* rewritten as

$$\mathcal{L}_1^w(\boldsymbol{\xi}, \mathbf{F}_p^{(0)}, \tilde{\boldsymbol{\xi}}) = 0, \quad (67a)$$

$$\mathcal{L}_2^w(\boldsymbol{\omega}, \mathbf{F}_p^{(0)}, \tilde{\boldsymbol{\omega}}) = 0, \quad (67b)$$

$$\mathcal{H}_1^w(\mathbf{u}^{(0)}, \mathbf{F}_p^{(0)}, \tilde{\mathbf{u}}^{(0)}) = 0, \quad (67c)$$

686 where  $\tilde{\boldsymbol{\xi}}$ ,  $\tilde{\boldsymbol{\omega}}$  and  $\tilde{\mathbf{u}}^{(0)}$  are test functions defined in certain Sobolev spaces, and  
 687  $\mathcal{L}_1^w$ ,  $\mathcal{L}_2^w$  and  $\mathcal{H}_1^w$  are suitable integral operators. Together with (67a)-(67c),  
 688 we rewrite in operatorial form also the homogenized problem (61) as

$$\mathcal{H}_2(\boldsymbol{\xi}, \boldsymbol{\omega}, \mathbf{u}^{(0)}, \mathbf{F}_p^{(0)}) = \mathbf{0}. \quad (68)$$

689 Note that (68) is not a weak form because the corresponding equation does  
 690 not involved spatial derivatives of  $\mathbf{F}_p^{(0)}$ .

691 *Second step.* We perform a backward Euler method [78] for discretizing the  
 692 evolution law for  $\mathbf{F}_p^{(0)}$  given by (68), thereby ending up with the following  
 693 system of time-discrete equations,

$$\mathcal{L}_{1[n]}^w(\boldsymbol{\xi}_{[n]}, \mathbf{F}_{p[n]}^{(0)}, \tilde{\boldsymbol{\xi}}) = 0, \quad (69a)$$

$$\mathcal{L}_{2[n]}^w(\boldsymbol{\omega}_{[n]}, \mathbf{F}_{p[n]}^{(0)}, \tilde{\boldsymbol{\omega}}) = 0, \quad (69b)$$

$$\mathcal{H}_{1[n]}^w(\mathbf{u}_{[n]}^{(0)}, \mathbf{F}_{p[n]}^{(0)}, \tilde{\mathbf{u}}^{(0)}) = 0, \quad (69c)$$

$$\mathcal{H}_{2[n]}(\boldsymbol{\xi}_{[n]}, \boldsymbol{\omega}_{[n]}, \mathbf{u}_{[n]}^{(0)}, \mathbf{F}_{p[n]}^{(0)}) = \mathbf{0}, \quad (69d)$$

694 where  $n = 1, \dots, N$  enumerates the nodes of a suitable time grid. We notice  
 695 that an explicit time discrete method could be also used. However, when  
 696 dealing with problems in Elastoplasticity, this election could lead to a less  
 697 accurate solution.

698 *Third step.* The operators  $\mathcal{L}_{1[n]}^w$ ,  $\mathcal{L}_{2[n]}^w$ ,  $\mathcal{H}_{1[n]}^w$  and  $\mathcal{H}_{2[n]}$ , are linear in  $\boldsymbol{\xi}_{[n]}$ ,  $\boldsymbol{\omega}_{[n]}$   
 699 and  $\mathbf{u}_{[n]}^{(0)}$ , respectively, but they are nonlinear in  $\mathbf{F}_{p[n]}^{(0)}$ . Thus, to search the  
 700 solution to (69a)-(69d), we linearize at each time step according to Newton's  
 701 method (with a linesearch). Therefore, at the  $k$ th iteration,  $k \in \mathbb{N}$ ,  $k \geq 1$ ,  
 702  $\mathbf{F}_{p[n,k]}^{(0)}$  is written as

$$\mathbf{F}_{p[n,k]}^{(0)} = \mathbf{F}_{p[n,k-1]}^{(0)} + \boldsymbol{\Psi}_{[n,k]}, \quad (70)$$

703 where  $\mathbf{F}_{p[n,k-1]}^{(0)}$  is known and  $\boldsymbol{\Psi}_{[n,k]}$  represents the unknown increment. We  
 704 introduce the notation

$$\mathcal{L}_{1[n,k-1]}^w(\boldsymbol{\xi}_{[n]}, \tilde{\boldsymbol{\xi}}) = \mathcal{L}_{1[n]}^w(\boldsymbol{\xi}_{[n]}, \mathbf{F}_{p[n,k-1]}^{(0)}, \tilde{\boldsymbol{\xi}}), \quad (71a)$$

$$\mathcal{L}_{2[n,k-1]}^w(\boldsymbol{\omega}_{[n]}, \tilde{\boldsymbol{\omega}}) = \mathcal{L}_{2[n]}^w(\boldsymbol{\omega}_{[n]}, \mathbf{F}_{p[n,k-1]}^{(0)}, \tilde{\boldsymbol{\omega}}), \quad (71b)$$

$$\mathcal{H}_{1[n,k-1]}^w(\mathbf{u}_{[n]}^{(0)}, \tilde{\mathbf{u}}_{[n]}^{(0)}) = \mathcal{H}_{1[n]}^w(\mathbf{u}_{[n]}^{(0)}, \mathbf{F}_{p[n,k-1]}^{(0)}, \tilde{\mathbf{u}}_{[n]}^{(0)}). \quad (71c)$$

705 Now, for each time step, and at the  $k$ th iteration, we solve

$$\mathcal{L}_{1[n,k-1]}^w(\boldsymbol{\xi}_{[n]}, \tilde{\boldsymbol{\xi}}) = 0, \quad (72a)$$

$$\mathcal{L}_{2[n,k-1]}^w(\boldsymbol{\omega}_{[n]}, \tilde{\boldsymbol{\omega}}) = 0, \quad (72b)$$

$$\mathcal{H}_{1[n,k-1]}^w(\mathbf{u}_{[n]}^{(0)}, \tilde{\mathbf{u}}^{(0)}) = 0, \quad (72c)$$

706 and obtain the “temporary” solutions  $\boldsymbol{\xi}_{[n,k-1]}$ ,  $\boldsymbol{\omega}_{[n,k-1]}$ , and  $\mathbf{u}_{[n,k-1]}^{(0)}$ , respec-  
707 tively. Then, upon setting

$$\mathcal{H}_{2[n,k-1]} = \mathcal{H}_{2[n]}(\boldsymbol{\xi}_{[n,k-1]}, \boldsymbol{\omega}_{[n,k-1]}, \mathbf{u}_{[n,k-1]}^{(0)}, \mathbf{F}_{p[n,k-1]}^{(0)}), \quad (73a)$$

$$\mathcal{H}_{[n,k-1]} = \mathcal{H}_{[n]}(\boldsymbol{\xi}_{[n,k-1]}, \boldsymbol{\omega}_{[n,k-1]}, \mathbf{u}_{[n,k-1]}^{(0)}, \mathbf{F}_{p[n,k-1]}^{(0)}), \quad (73b)$$

708 we linearize (69d), i.e.,

$$\mathcal{H}_{2[n,k-1]} + \mathcal{H}_{[n,k-1]} : \boldsymbol{\Psi}_{[n,k]} = \mathbf{0}, \quad (74)$$

709 where  $\mathcal{H}_{[n,k-1]}$  is a fourth-order tensor given by the Gâteaux derivative  
710 of  $\mathcal{H}_{2[n]}$ , computed with respect to its fourth argument, and evaluated in  
711  $\mathbf{F}_{p[n,k-1]}^{(0)}$ .

712 If the residuum  $\mathbf{F}_{p[n,k]}^{(0)}$  for  $k$  greater than, or equal to, a certain  $k_*$  is less  
713 than a tolerance  $\delta > 0$ , then we set  $\mathbf{F}_{p[n]}^{(0)} \equiv \mathbf{F}_{p[n,k_*]}^{(0)} = \mathbf{F}_{p[n,k_*-1]}^{(0)} + \boldsymbol{\Psi}_{[n,k_*]}$  and  
714 we regard it as the solution of Newton’s method. Thus, we compute  $\boldsymbol{\xi}_{[n]}$ ,  $\boldsymbol{\omega}_{[n]}$   
715 and  $\mathbf{u}_{[n]}^{(0)}$ .

716 These three steps are summarized in the algorithm 1.

## 717 7. Numerical results

718 In this section, the potentiality of our model, which is given by Equations  
719 (43), (45), (46) and (61), is shown by performing numerical simulations. In  
720 particular, we make the following considerations.

721 **(i) Geometry.** We consider the composite body  $\mathcal{B}^\varepsilon$  to have a layered three-  
722 dimensional structure, and we assume that the layers are orthogonal to the  
723 direction  $\boldsymbol{\mathcal{E}}_3$ , where  $\{\boldsymbol{\mathcal{E}}_A\}_{A=1}^3$  is an orthonormal basis of a system of Cartesian  
724 coordinates  $\{X_A\}_{A=1}^3$ . In this particular case, the material properties of  
725 the heterogeneous body only change along the  $\boldsymbol{\mathcal{E}}_3$  direction and, thus, they  
726 depend solely on the coordinate  $X_3$ . Consequently, the benchmark test at

---

**Algorithm 1**


---

```

1: procedure
2:   for  $n = 1, \dots, N$  do
3:     State  $k = 1$ 
4:     while  $e > \delta$  do (Known  $\mathbf{F}_{p[n,k-1]}^{(0)}$ )
5:       Solve  $\mathcal{L}_{1[n,k-1]}^w$  and  $\mathcal{L}_{2[n,k-1]}^w$  (To find  $\boldsymbol{\xi}_{[n,k-1]}$  and  $\boldsymbol{\omega}_{[n,k-1]}$ )
6:       Solve  $\mathcal{H}_{1[n,k-1]}^w$  (To find  $\mathbf{u}_{[n,k-1]}^{(0)}$ )
7:       Solve  $\mathcal{H}_{1[n,k-1]}^w$  (To find  $\boldsymbol{\Psi}_{[n,k]}$ )
8:        $\mathbf{F}_{p[n,k-1]}^{(0)} \leftarrow \mathbf{F}_{p[n,k-1]}^{(0)} + \boldsymbol{\Psi}_{[n,k]}$ 
9:       Compute  $e$ 
10:       $k = k + 1$ 
11:     end while
12:      $\mathbf{F}_{p[n]}^{(0)} = \mathbf{F}_{p[n,k-1]}^{(0)} + \boldsymbol{\Psi}_{[n,k]}$ 
13:     Solve  $\mathcal{L}_{1[n]}^w$  and  $\mathcal{L}_{2[n]}^w$  (To find  $\boldsymbol{\xi}_{[n]}$  and  $\boldsymbol{\omega}_{[n]}$ )
14:     Solve  $\mathcal{H}_{1[n]}^w$  (To find  $\mathbf{u}_{[n]}^{(0)}$ )
15:     Update micro and macro geometries
16:   end for
17: end procedure

```

---

727 hand can be recast into a one dimensional problem, that is, the reference  
728 configuration of the periodic cell and the body are considered to be the  
729 unidimensional domains  $\mathcal{Y}_0 = [0, \ell]$  and  $\mathcal{B}_h = [0, L]$ , respectively. We denote  
730 with  $\ell$  and  $L$ , respectively, the dimension of the periodic cell and the body  
731 along the direction  $\boldsymbol{\mathcal{E}}_3$ . Moreover, we suppose that the interface  $\Gamma_0$  is the  
732 middle point  $\ell/2$ , so that, each material under consideration has the same  
733 volume in the microscopic cell  $\mathcal{Y}_0$ .

734 *(ii) Material properties.* We prescribe the elasticity tensor  $\mathcal{C}^\varepsilon$  to be in-  
735 dependent on the macroscale variable  $X_3$ , i.e.  $\mathcal{C}^\varepsilon(X_3) = \mathcal{C}(X_3, Y_3) \equiv \mathcal{C}(Y_3)$ ,  
736 where  $\{Y_A\}_{A=1}^3$  is a system of microscale Cartesian coordinates. In addition,  
737 as stated above, we consider that the constituents of the heterogeneous ma-  
738 terial are isotropic, which implies that the non zero components of the  $6 \times 6$   
739 symmetric matrix representation of  $\mathcal{C}$  are given by

$$[\mathcal{C}]_{11} = [\mathcal{C}]_{22} = [\mathcal{C}]_{33} = \lambda + 2\mu, \quad (75a)$$

$$[\mathcal{C}]_{12} = [\mathcal{C}]_{13} = [\mathcal{C}]_{23} = \lambda, \quad (75b)$$

$$[\mathcal{C}]_{44} = [\mathcal{C}]_{55} = [\mathcal{C}]_{66} = \frac{1}{2}([\mathcal{C}]_{11} - [\mathcal{C}]_{12}) = \mu, \quad (75c)$$

740 where  $\lambda$  and  $\mu$  are Lamé's parameters. We suppose that  $\mathcal{C}$  is piece-wise  
 741 constant, which means that  $\lambda$  and  $\mu$  are defined as

$$\lambda(Y_3) = \begin{cases} \lambda_1, & \text{in } \mathcal{Y}_0^1 \\ \lambda_2, & \text{in } \mathcal{Y}_0^2 \end{cases} \quad \text{and} \quad \mu(Y_3) = \begin{cases} \mu_1, & \text{in } \mathcal{Y}_0^1 \\ \mu_2, & \text{in } \mathcal{Y}_0^2 \end{cases}. \quad (76)$$

742 Furthermore, we consider that  $\gamma$  has the same value in both constituents,  
 743 which means that it is already averaged.

744 **(iii) Plastic-like distortions.** We assume that the matrix representa-  
 745 tion of the tensor  $\mathbf{F}_p^{(0)}$  is diagonal with non-zero components  $[\mathbf{F}_p^{(0)}]_{11} = \frac{1}{\sqrt{p}}$ ,  
 746  $[\mathbf{F}_p^{(0)}]_{22} = \frac{1}{\sqrt{p}}$  and  $[\mathbf{F}_p^{(0)}]_{33} = p$ , where  $p$  is defined as the remodeling pa-  
 747 rameter. Furthermore, we restrict our investigation to the simpler case of  
 748  $\mathbf{F}_p^{(0)}$  depending solely on  $X_3$ . This means that, the plastic-like distortions of  
 749 order  $\varepsilon^0$  are, in a sense, already averaged, and thus variable from one cell  
 750 to the other, not inside them. In other words, we are interested in the pro-  
 751 duction of distortions in the tissue starting from the cell scale, rather than  
 752 from the cell's microstructure. This, of course, does not mean that the cell's  
 753 microstructure does not change.

754 Together with assumption (ii), we find that the  $6 \times 6$  matrix represen-  
 755 tation of the elasticity tensor, pulled-back to the reference configuration,  
 756 is symmetric, and its non-zero components are given by

$$[\mathcal{C}_R]_{11} = [\mathcal{C}_R]_{22} = (\lambda + 2\mu)p^2, \quad [\mathcal{C}_R]_{33} = (\lambda + 2\mu)p^{-4}, \quad (77a)$$

$$[\mathcal{C}_R]_{12} = \lambda p^2, \quad [\mathcal{C}_R]_{44} = [\mathcal{C}_R]_{55} = \mu p^{-1}, \quad (77b)$$

$$[\mathcal{C}_R]_{13} = [\mathcal{C}_R]_{23} = \lambda p^{-1}, \quad [\mathcal{C}_R]_{66} = \mu p^2. \quad (77c)$$

757 We remark that  $\mathcal{C}_R$  depends on  $X_3$  and time through  $p$ , whereas it inherits  
 758 the dependence of  $\mathcal{C}$  on the micro-scale variable,  $Y_3$ .

759 **(iv) Initial and boundary conditions.** In the present context, we im-  
 760 pose Dirichlet conditions for  $\mathbf{u}^{(0)}$  on the whole boundary  $\partial\mathcal{B}_h$ , i.e. we do not  
 761 consider a Neumann condition and therefore,  $\partial_u\mathcal{B}_h \equiv \partial\mathcal{B}_h$ . We note that,  
 762 although the homogenization process was developed for mixed boundary con-  
 763 ditions, the whole procedure stands, since the type of boundary conditions  
 764 does not play a role in the derivation of the homogenized model. In par-  
 765 ticular, we set  $[\mathbf{u}^{(0)}]_3 = 0$  at  $X_3 = 0$ , and  $[\mathbf{u}^{(0)}]_3 = \frac{u_L t}{t_f}$  at  $X_3 = L$ , where  
 766  $u_L$  is a target value for the displacement in the direction  $\mathcal{E}_3$ . Moreover,

767 we enforce an initial spatial distribution for the remodeling parameter  $p$  as  
 768  $p_{\text{in}}(X_3) = \alpha + \beta \cos(\frac{\pi}{L}X_3)$ , where  $\alpha$  and  $\beta$  are constants, such that  $p_{\text{in}}(X_3)$   
 769 is always strictly positive.

770 *7.1. Discussion of the numerical results*

771 Given the above considerations, we solve the following homogenized equa-  
 772 tions for  $\mathbf{u}^{(0)}$  and  $p$ ,

$$-\frac{\partial}{\partial X_3}([\hat{\mathcal{C}}_{\text{R}}]_{i3n3} \frac{\partial[\mathbf{u}^{(0)}]_n}{\partial X_3}) = \frac{\partial[\hat{\mathbf{D}}_{\text{R}}]_{i3}}{\partial X_3}, \quad \text{for } i = 1, 2, 3, \quad (78a)$$

$$\langle [\mathbf{C}_{\text{lin}}^{(0)}]_{33} \rangle \frac{\partial p}{\partial t} = \frac{\gamma}{3} \langle \text{dev}(\boldsymbol{\Sigma}_{\text{lin}}^{(0)}) \rangle p - \gamma \langle [\mathcal{C}_{\text{R}}]_{33nn} [\mathbf{E}_{\text{p}}]_{nn} ([\mathbf{C}_{\text{lin}}^{(0)}]_{33} - 1) \rangle p, \quad (78b)$$

773 The coefficients  $[\hat{\mathcal{C}}_{\text{R}}]_{ijkl}$ ,  $[\hat{\mathbf{D}}_{\text{R}}]_{ij}$  and  $[\mathbf{C}_{\text{lin}}^{(0)}]_{ij}$  are given by Equations (47a),  
 774 (47b) and (62), respectively, and are to be found by solving the auxiliary cell  
 775 problems for  $\boldsymbol{\xi}$  and  $\boldsymbol{\omega}$ , given by

$$-\frac{\partial}{\partial Y_3}([\mathcal{Q}]_{i3i3} \frac{\partial[\boldsymbol{\xi}]_{ik3}}{\partial Y_3}) = \frac{\partial[\mathcal{Q}]_{i3i3}}{\partial Y_3} \delta_{ik}, \quad \text{for } i, k = 1, 2, 3, \quad (79a)$$

$$-\frac{\partial}{\partial Y_3}([\mathcal{Q}]_{i3i3} \frac{\partial[\boldsymbol{\omega}]_i}{\partial Y_3}) = -\frac{\partial[\mathbf{Q}]_{33}}{\partial Y_3} \delta_{i3}, \quad \text{for } i = 1, 2, 3, \quad (79b)$$

776 with

$$[\mathcal{Q}]_{i3i3} = [\mathcal{C}_{\text{R}}]_{i3i3} - [\mathbf{Q}]_{33}, \quad [\mathbf{Q}]_{33} = [\mathcal{C}_{\text{R}}]_{33nn} [\mathbf{E}_{\text{p}}]_{nn}. \quad (80a)$$

777 In this work, we are not interested to address a real world situation. Our  
 778 aim is, instead, to show how the present theoretical framework can be numer-  
 779 ically simulated. For this reason, the parameters used in our computations  
 780 are arbitrarily chosen (see Table 1).

781 In Fig. 2, it is plotted the time evolution of the remodeling parameter  
 782  $p$  at two different points of the macroscopic domain, that is at  $X_3 = 7$  cm  
 783 and  $X_3 = 21$  cm. We observe that the evolution of  $p$  is quite different at  
 784 these two points. Indeed, at  $X_3 = 21$  cm,  $p$  increases and it is always greater  
 785 than one. On the contrary, at  $X_3 = 7$  cm, it is monotonically decreasing  
 786 and tends to be lower than one. In Fig. 3, we show the spatial profile of the  
 787 effective coefficients  $[\hat{\mathcal{C}}]_{33}$ ,  $[\hat{\mathcal{C}}_{\text{R}}]_{33}$  and  $[\hat{\mathbf{D}}_{\text{R}}]_{33}$ . The effective coefficient  $[\hat{\mathcal{C}}]_{33}$   
 788 (see Remark 3) can be computed by using the analytical formula (see e.g.  
 789 [56, 69]),



Parameter	Unit	Value	Parameter	Unit	Value
$L$	[cm]	28.000	$\lambda_1$	[Pa]	1.00
$u_L$	[cm]	1.0000	$\lambda_2$	[Pa]	2.00
$\gamma$	[1/s]	1.0000	$\mu_1$	[Pa]	0.10
$\alpha$	[-]	1.0035	$\mu_2$	[Pa]	0.06
$\beta$	[-]	-0.0035	$t_0$	[s]	0.00
$N$	[-]	4.0000	$t_f$	[s]	10.0

Table 1: Parameters used in the numerical simulations.

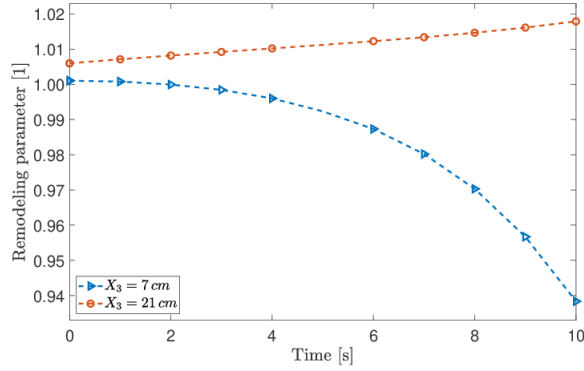


Figure 2: Evolution of the remodeling parameter  $p$  at two different points ( $X_3 = 7$  cm and  $X_3 = 21$  cm) of the macroscopic domain.

$$\begin{aligned}
[\hat{\mathcal{C}}]_{ijkl} = & \langle [\mathcal{C}]_{ijkl} - [\mathcal{C}]_{ijp3}([\mathcal{C}]_{p3s3})^{-1}[\mathcal{C}]_{s3kl} \rangle \\
& + \langle [\mathcal{C}]_{ijp3}([\mathcal{C}]_{p3s3})^{-1} \rangle \langle ([\mathcal{C}]_{s3t3})^{-1} \rangle^{-1} \langle ([\mathcal{C}]_{t3m3})^{-1}[\mathcal{C}]_{m3kl} \rangle. \quad (81)
\end{aligned}$$

790 We observe that even if a loading ramp condition has been imposed on  $\mathbf{u}^{(0)}$   
791 at the border  $X_3 = L$ , the effective coefficient  $[\hat{\mathcal{C}}]_{33}$  does not vary on time.  
792 This is because, in contrast to the case in which the plastic-like distortions  
793 are accounted for, the cell and homogenized problems (cf. (48) and (49)) are  
794 decoupled. On the other hand, the pulled-back effective coefficients  $[\hat{\mathcal{C}}_{\text{R}}]_{33}$   
795 and  $[\hat{\mathbf{D}}_{\text{R}}]_{33}$ , given by Equations (47a) and (47b), respectively, do change in  
796 time since their equations are coupled with an evolution one and, as it can  
797 be observed, they are strongly influenced by the initial distribution of  $p$ . In  
798 fact, at the spatial point  $X_3 = 21$  cm, that is, when  $p > 1$ ,  $[\hat{\mathcal{C}}_{\text{R}}]_{33}$  decreases

799 and  $[\hat{\mathbf{D}}_R]_{33}$  increases with time. The contrary occurs at  $X_3 = 7$  cm, i.e. when  
 800  $p < 1$ .

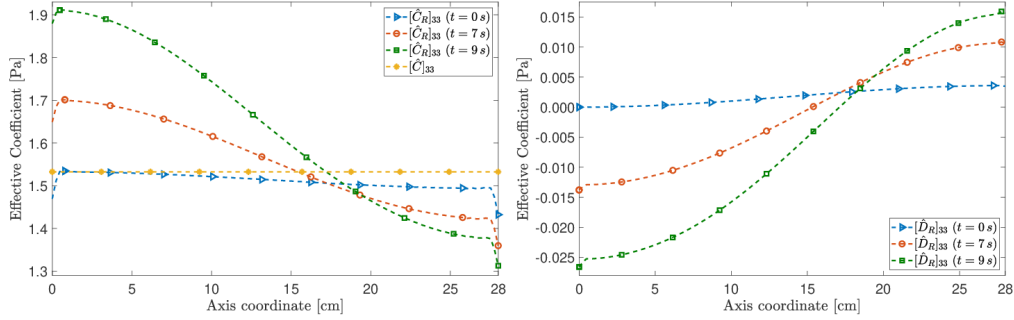


Figure 3: Spatial distribution of the effective coefficients  $[\hat{\mathcal{C}}]_{33}$ ,  $[\hat{\mathcal{C}}_R]_{33}$  and  $[\hat{\mathbf{D}}_R]_{33}$  at different time instants.

801 Additionally, in Fig. 4 it is illustrated the third component of the macroscopic leading order term of the displacement  $\mathbf{u}^\varepsilon$  at three different time  
 802 instants. Particularly, we plot the numerical solution of the homogenized  
 803 problems (46) and (49), represented with  $[\mathbf{u}_R^{(0)}]_3$  and  $[\mathbf{u}^{(0)}]_3$ , respectively. We  
 804 note that, as expected from our election of the boundary condition, the displacement  
 805 component increases monotonically in time. However, we notice  
 806 that the introduction of the plastic-like distortions has a direct impact on the  
 807 displacement distribution in the interior macroscopic points. Specifically, in  
 808 these points the displacement has a higher magnitude.  
 809

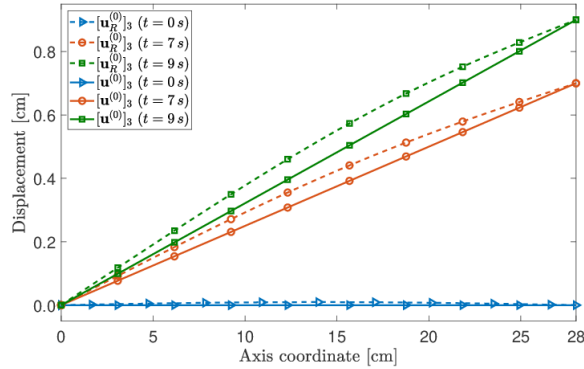


Figure 4: Spatial distribution of the macroscopic leading order term of the displacement with remodeling ( $[\mathbf{u}_R^{(0)}]_3$ ) and without remodeling ( $[\mathbf{u}^{(0)}]_3$ ).

810 The situation described in our numerical simulations, although simplified,

811 could be a good starting point in the study of the remodeling of biological  
812 tissues. For example, the geometrical properties of bone's osteons permit to  
813 model them as layered composites (see e.g. [69]).

## 814 **8. Concluding remarks**

815 In the present work, we studied the dynamics of a heterogeneous material,  
816 constituted by two hyperelastic media with evolving micro-structure, by the  
817 application of the asymptotic homogenization technique. The evolution of  
818 the micro-structure of the composite media was characterized through the  
819 development of plastic-like distortions, which were described by means of the  
820 BKL decomposition.

821 The asymptotic homogenization method was applied to a set of problems  
822 comprising a scale-dependent, quasi-static law of balance of linear momentum  
823 and an evolution law for the tensor of plastic-like distortions. After obtaining  
824 the local and homogenized problems, we rewrote them by considering the De  
825 Saint-Venant strain energy density within the limit of small deformations.  
826 Although the selection of the strain energy density was due to its simplicity,  
827 it is helpful for the description of remodeling processes undergoing small  
828 deformations. For instance, this could be the case for describing bone aging.  
829 Then, the theoretical setting developed in the present work is applicable  
830 (Elastoplasticity is actually quite appropriate to model the bone [73]). In  
831 such a case, appropriate constitutive laws describing the progression of the  
832 material properties should be found based on experimental literature (e.g.  
833 [35]). Nevertheless, for studying a larger range of problems, we need to select  
834 nonlinear constitutive laws and write the corresponding cell and homogenized  
835 problems.

836 As a consequence of the introduction of the tensor of plastic distortions,  
837 two independent cell problems were inferred, which reduce to the classical cell  
838 problems encountered in the homogenization of linear problems in elastostat-  
839 ics. Moreover, we proposed an evolution equation for the inelastic distortions  
840 describing a remodeling process. Such evolution law models a stress-driven  
841 production of inelastic distortions, as the one that is often encountered in  
842 studies of inelastic processes constructed on the decomposition given by (5)  
843 [78]. The evolution law is suitable for the case of finite strain Elastoplastic-  
844 ity, and for the case of remodeling of biological tissues. Finally, we outlined  
845 a computational procedure in order to solve the up-scaled problems and we  
846 performed numerical simulations for a particular case of a layered composite

847 body. Besides, we assumed that the leading order term of the asymptotic  
848 expansion of the tensor of plastic distortions,  $\mathbf{F}_p^{(0)}$ , depends only on the  
849 macro-scale variable  $X$ . This consideration, however, might be relaxed by  
850 allowing  $\mathbf{F}_p^{(0)}$  to take into account the heterogeneities of the composite mate-  
851 rial through the microscopic spatial variable  $Y$ . The numerical results showed  
852 the influence of the plastic-like distortions on both the effective coefficients  
853 and the macroscopic leading order term of the displacement.

854 As future work, we intend to deal with the resolution of a particular  
855 problem, like for instance the modeling of bones [49], tumor growth [67, 2,  
856 43, 52, 70, 71], or tissue aging [20]. A further step could be the study, with  
857 the aid of the Homogenization Theory, of the coupling between the results  
858 presented in this work and the fluid flow in a hydrated tissue, or in the case  
859 of wavy laminar structures.

## 860 Acknowledgments

861 AR has been funded by the *Istituto Nazionale di Alta Matematica* "Francesco  
862 Saveri" (National Institute for High Mathematics "Francesco Saveri") through  
863 a research project MATHTECH-CNR-INdAM and is currently employed in  
864 the research project "Mathematical multi-scale modeling of biological tis-  
865 sues" (N. 64) financed by the Politecnico di Torino (Scientific Advisor: Alfio  
866 Grillo).. RR gratefully acknowledges the "Proyecto Nacional de Ciencias  
867 Básicas No. 7515, Cuba 2015–2018. JM and RP acknowledge support from  
868 the Ministry of Economy in Spain (project reference DPI2014-58885-R).

## 869 Declaration of interest

870 The Authors declare that they have no conflict of interest.

## 871 Article information

872 DOI: 10.1016/j.ijnonlinmec.2018.06.012. Available online: July 2, 2018  
873 Journal: *International Journal of Non-Linear Mechanics* 106 (2018) 245-257

## 874 Bibliography

- 875 [1] Allaire, G., Briane, M. (1996). *Multiscale convergence and reiterated*  
876 *homogenisation*. Proceedings of the Royal Society of Edinburgh: Section  
877 A Mathematics 126:297-342.

- 878 [2] Ambrosi, D., Mollica, F. (2002). *On the mechanics of a growing tumor*.  
879 International Journal of Engineering Science 40:1297-1316.
- 880 [3] Ambrosi, D., Guana, F. (2007). *Stress-modulated growth*. Mathematics  
881 and Mechanics of Solids 12:319-342.
- 882 [4] Auriault, J. L., Boutin, C., Geindreau, C. (2009). *Homogenization of*  
883 *Coupled Phenomena in Heterogenous Media*. ISTE, London, UK; J. Wi-  
884 ley, New Jersey, EE. UU.
- 885 [5] Bakhvalov, N., Panasenko, G. (1989). *Homogenization: Averaging pro-*  
886 *cesses in periodic media*. Kluwer, Dordrecht, The Netherlands.
- 887 [6] Benveniste, Y. (2006). *A general interface model for a three-dimensional*  
888 *curved thin anisotropic interphase between two anisotropic media*. Jour-  
889 nal of the Mechanics and Physics of Solids, 54(4):708-734.
- 890 [7] Benveniste, Y. and Miloh, T. (2001). *Imperfect soft and stiff interfaces*  
891 *in two-dimensional elasticity*. Mechanics of Materials, 33(6):309-323.
- 892 [8] Bensoussan, A., Lions, J.-L., Papanicolaou, G. (1978). *Asymptotic Anal-*  
893 *ysis for Periodic Structures*. AMS Chelsea Publishing.
- 894 [9] Burridge, R., Keller, J. B. (1981). *Poroelasticity equations derived*  
895 *from microstructure*. The Journal of the Acoustical Society of Amer-  
896 ica 70:1140-1146.
- 897 [10] Byrne, H. (2003). *Modelling avascular tumour growth* in L. Preziosi Ed.  
898 *Cancer modelling and simulations*. Chapman & Hall/CRC.
- 899 [11] Castañeda, P. P. (1991). *The effective mechanical properties of nonlinear*  
900 *isotropic composites*. Journal of the Mechanics and Physics of Solids  
901 39:45-71.
- 902 [12] Cermelli, P., Fried, E., Sellers, S. (2001). *Configurational stress, yield*  
903 *and flow in rate-independent plasticity*. Proceedings of the Royal Society  
904 A 457:1447-1467.
- 905 [13] Ciarletta, P., Destrade, M., and Gower, A. L. (2016). *On residual*  
906 *stresses and homeostasis: an elastic theory of functional adaptation in*  
907 *living matter*. Scientific Reports, 6(1).

- 908 [14] Cioranescu, D., Donato, P. (1999). *An Introduction to Homogenization*.  
909 Oxford University Press Inc., New York, EE. UU.
- 910 [15] Collis, J., Brown, D. L., Hubbard, M. E., O’Dea, R. D. (2017). *Effective*  
911 *equations governing an active poroelastic medium*. Proceedings of the  
912 Royal Society A 473:20160755.
- 913 [16] Cowin, S. C. (2000). *How is a tissue built?* Journal of Biomechanical  
914 Engineering, 122(6):553.
- 915 [17] Curnier, A., He, Q.-C., Zysset, P. (1995). *Conewise linear elastic mate-*  
916 *rials*. Journal of Elasticity 37:1-38.
- 917 [18] Di Carlo, A., Quiligotti, S. (2002). *Growth and balance*. Mechanics Re-  
918 search Communications 29:449-456.
- 919 [19] Di Stefano, S., Carfagna, M., Knodel, M. M., Hashlamoun, K., Federico  
920 S., Grillo A. *Anelastic reorganisation in fibre-reinforced biological tissues*.  
921 Submitted.
- 922 [20] Epstein, M. (2009). *The split between remodelling and aging*. Interna-  
923 tional Journal of Non-Linear Mechanics 44.
- 924 [21] Epstein, M., Elżanowski, M. (2007). *Material inhomogeneities and their*  
925 *evolution. A geometric approach*. Springer-Verlag Berlin Heidelberg.
- 926 [22] Epstein, M., Maugin, G. A. (1996). *On the geometrical material struc-*  
927 *ture of anelasticity*. Acta Mechanica 115.
- 928 [23] Epstein, M., Maugin, G. A. (2000). *Thermomechanics of volumetric*  
929 *growth in uniform bodies*. International Journal of Plasticity 16:951-978.
- 930 [24] Fang, Z., Yan, C., Sun, W., Shokoufandeh, A., Regli, W. (2005). *Homog-*  
931 *enization of heterogeneous tissue scaffold: A comparison of mechanics,*  
932 *asymptotic homogenization, and finite element approach*. Applied Bion-  
933 ics and Biomechanics 2:17-29.
- 934 [25] Federico, S. (2012). *Covariant formulation of the tensor algebra of non-*  
935 *linear elasticity*. International Journal of Non-Linear Mechanics 47:273-  
936 284.

- 937 [26] Ganghoffer, J.-F. (2010). *On Eshelby tensors in the context of thermo-*  
938 *dynamics of open systems: Applications to volumetric growth.* Interna-  
939 tional Journal of Engineering Science 48:2081-2098.
- 940 [27] Ganghoffer, J.-F. (2013). *A kinematically and thermodynamically con-*  
941 *sistent volumetric growth model based on the stress-free configuration.*  
942 International Journal of Solids and Structures 50:3446-3459.
- 943 [28] Gei, M., Genna, F., Bigoni, D. (2002). *An Interface Model for the Peri-*  
944 *odontal Ligament.* Journal of Biomechanical Engineering, 124(5):538.
- 945 [29] Givero, C., Preziosi, L. (2012). *Modelling the compression and reorga-*  
946 *nization of cell aggregates.* Mathematical Medicine and Biology 29:181-  
947 204.
- 948 [30] Goriely, A. (2017). *The Mathematics and Mechanics of Biological*  
949 *Growth.* Springer.
- 950 [31] Grillo, A., Prohl, R., Wittum, G. (2015). *A generalised algorithm for*  
951 *anelastic processes in elastoplasticity and biomechanics.* Mathematics  
952 and Mechanics of Solids 22:502-527.
- 953 [32] Grillo, A., Carfagna, M. Federico, S. (2018). *An Allen-Cahn approach*  
954 *to the remodelling of fibre-reinforced anisotropic materials.* Journal of  
955 Engineering Mathematics (In Press).
- 956 [33] Grillo, A., Federico, S., Wittum, G. (2012). *Growth, mass transfer and*  
957 *remodelling in fibre-reinforced multi-constituent materials.* International  
958 Journal of Non-Linear Mechanics 47:388-401.
- 959 [34] Grillo, A., Prohl, R., Wittum, G. (2016). *A poroplastic model of struc-*  
960 *tural reorganisation in porous media of biomechanical interest.* Contin-  
961 uum Mechanics and Thermodynamics 28:579-601.
- 962 [35] Grynpas, M. (1993). *Age and disease-related changes in the mineral of*  
963 *bone.* Calcified Tissue International 53:57-64.
- 964 [36] Guinovart-Díaz, R., Rodríguez-Ramos, R., Bravo-Castillero, J., López-  
965 Realpozo, J., Sabina, F., Sevostianov, I. (2013). *Effective elastic prop-*  
966 *erties of a periodic fiber reinforced composite with parallelogram-like ar-*  
967 *rangement of fibers and imperfect contact between matrix and fibers.* In-  
968 ternational Journal of Solids and Structures, 50(13):2022-2032.

- 969 [37] Hammer, D. A. and Tirrell, M. (1996). *Biological adhesion at interfaces*.  
970 Annual Review of Materials Science, 26(1):651-691.
- 971 [38] Hashin, Z. (1990). *Thermoelastic properties of fiber composites with im-*  
972 *perfect interface*. Mechanics of Materials, 8(4):333-348.
- 973 [39] Hashin, Z. (2002). *Thin interphase/imperfect interface in elasticity with*  
974 *application to coated fiber composites*. Journal of the Mechanics and  
975 Physics of Solids, 50(12):2509-2537.
- 976 [40] Holmes, M. H. (1995). *Introduction to perturbation methods* (Vol. 20).  
977 Springer Science & Business Media, Springer-Verlag, New York.
- 978 [41] Hori, M., Nemat-Nasser, S. (1999). *On two micromechanics theories for*  
979 *determining micro-macro relations in heterogeneous solids*. Mechanics  
980 of Materials 31:667-682.
- 981 [42] Javili, A., Steinmann P., Kuhl, E. (2014). *A novel strategy to identify*  
982 *the critical conditions for growth-induced instabilities*. Journal of the  
983 Mechanical Behavior of Biomedical Materials 29:20-32.
- 984 [43] Jain, R. K., Martin, J. D., Stylianopoulos, T. (2014). *The role of me-*  
985 *chanical forces in tumor growth and therapy*. Annual Review of Biomed-  
986 ical Engineering 16:321-346.
- 987 [44] Olsson, T., Klarbring, A. (2008). *Residual stresses in soft tissue as a*  
988 *consequence of growth and remodeling: application to an arterial geom-*  
989 *etry*. European Journal of Mechanics A/Solids 27:959-974.
- 990 [45] Kuhl, E., Holzapfel, G.A. (2007). *A continuum model for remodeling in*  
991 *living structures*. Journal of Material Science 42:8811-8823.
- 992 [46] Lefik, M., Schrefler, B. (1996). *Fe modelling of a boundary layer cor-*  
993 *rector for composites using the homogenization theory*. Engineering with  
994 Computers 13:31-42.
- 995 [47] Leyrat, A., Duperray, A., Verdier, C. (2003). *Cancer Modelling and*  
996 *Simulation*, chapter *Adhesion Mechanisms in Cancer Metastasis* Ed.  
997 L. Preziosi. Chapman & Hall/CRC Mathematical and Computational  
998 Biology.



- 999 [48] Lin, W. J., Iafrati, M. D., Peattie, R. A., and Dorfmann, L. (2018).  
1000 *Growth and remodeling with application to abdominal aortic aneurysms.*  
1001 *Journal of Engineering Mathematics*, 109(1):113-137.
- 1002 [49] Lu, Y., Lekszycki, T. (2016). *Modelling of bone fracture healing: in-*  
1003 *fluence of gap size and angiogenesis into bioresorbable bone substitute.*  
1004 *Mathematics and Mechanics of Solids* 22:1997-2010.
- 1005 [50] Lubliner, J. (2008). *Plasticity Theory (Dover Books on Engineering).*  
1006 Dover Publications.
- 1007 [51] Lukkassen, D., Milton, G. W. (2002). *On hierarchical structures and*  
1008 *reiterated homogenization.* *Function Spaces, Interpolation Theory and*  
1009 *Related Topics* 355-368.
- 1010 [52] Mascheroni, P., Carfagna, M., Grillo, A., Boso, D. P., Schrefler, B.  
1011 A. (2018). *An avascular tumor growth model based on porous media*  
1012 *mechanics and evolving natural states.* *Mathematics and Mechanics of*  
1013 *Solids* DOI: 10.1177/1081286517711217 (In press).
- 1014 [53] Marsden, J. E., Hughes, T. J. R. (1983). *Mathematical Foundations of*  
1015 *Elasticity.* Dover Publications Inc., New York.
- 1016 [54] Maugin, G. A., Epstein, M. (1998). *Geometrical material structure of*  
1017 *elastoplasticity.* *International Journal of Plasticity* 14:109-115.
- 1018 [55] Mićunović, M. V. (2009). *Thermomechanics of Viscoplasticity - Funda-*  
1019 *mentals and Applications.* Springer, Heidelberg, Germany
- 1020 [56] Milton, G. W. (2002). *The Theory of Composites.* Cambridge University  
1021 Press .
- 1022 [57] Panasenko, G. (2005). *Multi-Scale Modelling for Structures and Com-*  
1023 *posites.* Springer, Berlin.
- 1024 [58] Parnell, W. J., Vu, M. V., Grimal, Q., Naili, S. (2012). *Analytical meth-*  
1025 *ods to determine the effective mesoscopic and macroscopic elastic prop-*  
1026 *erties of cortical bone.* *Biomechanics and Modeling in Mechanobiology*  
1027 11:883-901.

- 1028 [59] Penta, R., Ambrosi, D. (2014). *Effective governing equations for poroe-*  
1029 *lastic growing media*. Quarterly Journal of Mechanics and Applied Math-  
1030 ematics 67:69-91.
- 1031 [60] Penta, R., Gerisch, A. (2015). *Investigation of the potential of asymptotic*  
1032 *homogenization for elastic composites via a three-dimensional computa-*  
1033 *tional study*. Computing and Visualization in Science 17:185-201.
- 1034 [61] Penta, R., Gerisch, A. (2017). *The asymptotic homogenization elasticity*  
1035 *tensor properties for composites with material discontinuities*. Contin-  
1036 uum Mechanics and Thermodynamics 29:187-206.
- 1037 [62] Penta, R., Gerisch, A. (2018). *An Introduction to Asymptotic homoge-*  
1038 *nization* in Gerisch, A., Penta, R., Lang., J (eds.) *Multiscale models in*  
1039 *Mechano and Tumor Biology*, Lecture Notes in Computational Science  
1040 and Engineering (122), Springer.
- 1041 [63] Penta, R., Merodio, J. (2017). *Homogenized modeling for vascularized*  
1042 *poroelastic materials*. Meccanica 52:3321-3343.
- 1043 [64] Penta, R., Ramírez-Torres, A., Merodio, J., Rodríguez-Ramos, R.  
1044 (2018). *Effective balance equations for elastic composites subject to in-*  
1045 *homogeneous potentials*. Continuum Mechanics and Thermodynamics  
1046 30:145-163.
- 1047 [65] Penta, R., Raum, K., Grimal, Q., Schrof, S., Gerisch, A. (2016). *Can a*  
1048 *continuous mineral foam explain the stiffening of aged bone tissue? A*  
1049 *micromechanical approach to mineral fusion in musculoskeletal tissues*.  
1050 *Bioinspiration & Biomimetics* 11:035004.
- 1051 [66] Persson, L. E., Persson, L., Svanstedt, N., Wyller, J. (1993). *The ho-*  
1052 *mogenization method. An introduction*. Studentlitteratur, Lund.
- 1053 [67] Preziosi, L., Vitale, G. (2011). *A multiphase model of tumor and tissue*  
1054 *growth including cell adhesion and plastic reorganization*. Mathematical  
1055 Models and Methods in Applied Sciences 21:1901-1932.
- 1056 [68] Pruchnicki, E. (1998). *Hyperelastic homogenized law for reinforced elas-*  
1057 *tomer at finite strain with edge effects*. Acta Mechanica 129:139-162.

- 1058 [69] Ramírez-Torres, A., Penta, R., Rodríguez-Ramos, R., Merodio, J.,  
1059 Sabina, F. J., Bravo-Castillero, J., Guinovart-Díaz, R., Preziosi, L.,  
1060 Grillo, A. (2018). *Three scales asymptotic homogenization and its ap-*  
1061 *plication to layered hierarchical hard tissues*. International Journal of  
1062 Solids and Structures 130-131:190-198.
- 1063 [70] Ramírez-Torres, A., Rodríguez-Ramos, R., Merodio, J., Bravo-  
1064 Castillero, J., Guinovart-Díaz, R., Alfonso, J. C. L. (2015). *Action of*  
1065 *body forces in tumor growth*. International Journal of Engineering Sci-  
1066 ence 89:18-34.
- 1067 [71] Ramírez-Torres, A., Rodríguez-Ramos, R., Merodio, J., Bravo-  
1068 Castillero, J., Guinovart-Díaz, R., Alfonso, J. C. L. (2015). *Mathemati-*  
1069 *cal modeling of anisotropic avascular tumor growth*. Mechanics Research  
1070 Communications 69:8-14.
- 1071 [72] Reimer, P., Parizel, P. M., Meaney, J. F. M., Stichnoth, F. A., editors  
1072 (2010). *Clinical MR Imaging*. Springer Berlin Heidelberg.
- 1073 [73] Ritchie, R. O., Buehler, M. J., Hansma, P. (2009). *Plasticity and tough-*  
1074 *ness in bone*. Physics Today 62:41-47.
- 1075 [74] Rohan, E., Cimrman, R., Lukeš, V. (2006). *Numerical modelling and*  
1076 *homogenized constitutive law of large deforming fluid saturated hetero-*  
1077 *geneous solids*. Composites and Structures 84:1095-1114.
- 1078 [75] Rohan, E., Lukeš, V. (2010). *Microstructure based two-scale modelling*  
1079 *of soft tissues*. Mathematics and Computers in Simulation 80:1289-1301.
- 1080 [76] Rodriguez, E. K., Hoger, A., McCulloch, A. D. (1994). *Stress-dependent*  
1081 *finite growth in soft elastic tissues*. Journal of Biomechanics 27:455-467.
- 1082 [77] Sanchez-Palencia, E. (1980). *Non-homogeneous media and vibration the-*  
1083 *ory*. In: Lecture Notes in Physics, 127. Springer-Verlag, Berlin.
- 1084 [78] Simo, J. C., Hughes, T. J. R. (1988). *Computational Plasticity*. Springer,  
1085 New York.
- 1086 [79] Suquet, P. (1987). *Elements of homogenization for inelastic solid me-*  
1087 *chanics in Homogenization techniques for composite media*. Eds. E.  
1088 Sanchez-Palencia and A. Zaoui. Springer-Verlag, Berlin.

- 1089 [80] Taber, L. A. (1995). *Biomechanics of growth, remodeling, and morpho-*  
1090 *genesis*. Applied Mechanics Reviews, 48(8):487.
- 1091 [81] Taffetani, M., de Falco, C., Penta, R., Ambrosi, D., Ciarletta, P. (2014).  
1092 *Biomechanical modelling in nanomedicine: multiscale approaches and*  
1093 *future challenges*. Archive of Applied Mechanics 84:1627-1645.
- 1094 [82] Telega, J. J., Galka, A., Tokarzewski, S. (1999). *Application of the reit-*  
1095 *erated homogenization to determination of effective moduli of a compact*  
1096 *bone*. Journal of Theoretical and Applied Mechanics 37(3):687-706.
- 1097 [83] Tsalis, D., Baxevanis, T., Chatzigeorgiou, G., Charalambakis, N. (2013).  
1098 *Homogenization of elastoplastic composites with generalized periodicity*  
1099 *in the microstructure*. International Journal of Plasticity 51:161-187.
- 1100 [84] Walpole, L. J. (1981). *Elastic behaviour of composites materials: theo-*  
1101 *retical foundations*. Advances in Applied Mechanics 21:169-242.
- 1102 [85] Walpole, L. J. (1984). *Fourth-rank tensors of the thirty two crys-*  
1103 *tal classes: multiplication tables*. Proceedings of the Royal Society A  
1104 391:149-179.
- 1105 [86] <https://en.wikipedia.org/wiki/plasticity> (physics)