International Journal of Non-Linear Mechanics 47 (2012) 248–257

Contents lists available at ScienceDirect

International Journal of Non-Linear Mechanics

journal homepage: www.elsevier.com/locate/nlm

Growth instabilities and folding in tubular organs: A variational method in non-linear elasticity ☆

P. Ciarletta [a,*], M. Ben Amar [b]

[a] CNRS and Université Pierre et Marie Curie - Paris 6, Institut Jean le Rond d'Alembert, UMR CNRS 7190, 4 place Jussieu, Case 162, 75005 Paris, France
[b] Laboratoire de Physique Statistique, Ecole Normale Supérieure, UPMC Univ Paris 06, Université Paris Diderot, UMR CNRS 8550, 24 rue Lhomond, 75005 Paris, France

ARTICLE INFO

Available online 24 June 2011

Keywords:
Volumetric growth
Bifurcation analysis
Canonical transformation
Non-linear elasticity
Tissue folding
Morphogenesis

ABSTRACT

Morphoelastic theories have demonstrated that elastic instabilities can occur during the growth of soft materials, initiating the transition toward complex patterns. Within the framework of non-linear elasticity, the theory of incremental elastic deformations is classically employed for solving stability problems with finite strains. In this work, we define a variational method to study the bifurcation of growing cylinders with circular section. Accounting for a constant axial pre-stretch, we define a set of canonical transformations in mixed polar coordinates, providing a locally isochoric mapping. Introducing a generating function to derive an implicit gradient form of the mixed variables, the incompressibility constraint for the elastic deformation is solved exactly. The canonical representation allows to transform a generic boundary value problem, characterized by conservative body forces and surface traction loads, into a completely variational formulation. The proposed variational method gives a straightforward derivation of the linear stability analysis, which would otherwise require lengthy manipulations on the governing incremental equations. The definition of a generating function can also account for the presence of local singularities in the elastic solution. Bifurcation analysis is performed for few constrained growth problems of biomechanical interests, such as the mucosal folding of tubular tissues and surface instabilities in tumor growth. In a concluding section, the theoretical results are discussed for clarifying how anisotropy, residual strains and external constraints can affect the stability properties of soft tissues in growth and remodeling processes.

1. Introduction

The emergence of shapes in living matter is the final result of a series of complex interactions which relate the biochemical processes driving changes of microstructure to the macroscopic reorganization of the material architecture. Understanding the basic principles and the key mechanisms coordinating such a crosstalk at different length-scales is one of the main challenges in developmental biology [1,2]. From a biomechanical perspective, a great interest is given to the investigation of the role played by the non-linear elastic properties in the formation of a specific pattern (see the reviewing works of Taber [3,4], and references therein). In the last years, a number of morphoelastic theories have been formulated in order to identify the mechanical feedbacks regulating growth and remodeling in biological materials [5–7]. The results of a wide variety of theoretical studies, ranging from continuum to discrete models, demonstrate that the transition toward a more complex pattern for soft materials is often initiated by a mechanical instability [8–11].

In this work, we will focus on the bifurcation analysis of soft growing materials with circular section, with the aim to investigate the influence both of growth and of external constraints (intended in terms of applied traction loads and/or spatial confinement). The circular geometry is chosen to describe the growth pattern of multilayered tubular organs, such as airways [12], oesophagus [13], intestine [14] and blood vessels [15]. Incompatible growth processes between the layers result in a complex transmural distribution of residual strains inside the tissue, whose determination is essential for biomedical applications [16]. Furthermore, the inner mucosal layer in physiological conditions is often characterized by the appearance of folds, even in absence of external loading [17]. In pathological conditions, an abnormal thickening of the tissue layers can determine significant changes in the observed patterns of mucosal folding, which, in turn, may also affect the mechanical integrity and the biological function of the tissues [18]. In addition, detection of contour instabilities is of utmost importance in the early diagnosis of skin cancer, where the loss of circularity of the tumor mass is driven by a competition between elasticity and nutrient diffusion [19]. A loss of symmetry in circular fronts is also correlated to the aggressiveness of other neoplasia, as reported for glioma tumor cells [20] and for the fibrotic tissue in tumor cords [21]. Other than the mentioned clinical interest, a quantification of the effects

☆ Dedicated to Ray W. Ogden on the occasion of his 65th birthday.

* Corresponding author.
E-mail address: ciarletta@dalembert.upmc.fr (P. Ciarletta).

0020-7462/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ijnonlinmec.2011.05.013

of growth on the stability of soft materials is paramount for applications in bioengineering [22] and in biomaterials [23].

In the following, we define a completely variational method for investigating the growth instabilities and the folding of tubular organs. The classical approach using incremental elastic deformation is resumed in Section 2, reporting the governing equations for an incompressible, hyperelastic material. In Section 3, we transform the incremental boundary value problem into a fully variational formulation for the elastic growth. A scalar generating function is defined to ensure the canonical transformation of a local isochoric mapping. Bifurcation analysis, based on the proposed variational method, is performed in Section 4 for few problems of constrained growth. Finally, the results of the linear stability analysis are discussed in Section 5, identifying the advantages and the limitations of the variational approach with respect to the classical incremental method.

2. Method of incremental elastic deformations

The equations of incremental deformations for elastic cylinders with circular section have been proposed by Haughton and Ogden in a couple of articles investigating the stability of incompressible membranes [24] and thick-walled tubes [25]. Their fundamental idea is to consider an infinitesimal change of the deformation mapping from $\mathbf{x}=\boldsymbol{\chi}(\mathbf{X})$ to $\mathbf{x}'=\boldsymbol{\chi}'(\mathbf{X})$, defined as

$$\delta\mathbf{x}=\delta\boldsymbol{\chi}=\boldsymbol{\chi}'(\mathbf{X})-\boldsymbol{\chi}(\mathbf{X}) \tag{1}$$

Considering displacement terms of order $|\delta\mathbf{x}|^2$ and higher negligible, then $\delta\mathbf{x}$ can be regarded as an incremental deformation with respect to the configuration mapped by $\chi(\mathbf{X})$. Choosing to express such incremental deformation as a function of the actual position $\mathbf{x}$, from standard vectorial algebra the deformation gradient $\mathbf{F}$ can be defined as follows:

$$\mathbf{F}=\frac{d\mathbf{x}'}{d\mathbf{X}}=\frac{d\mathbf{x}}{d\mathbf{X}}+\frac{d(\delta\mathbf{x})}{d\mathbf{x}}\frac{d\mathbf{x}}{d\mathbf{X}}=\mathbf{F}^{(0)}+\delta\mathbf{F}\mathbf{F}^{(0)} \tag{2}$$

while the incremental volume δJ is given at first order by

$$\delta J=J\delta\mathbf{F}\mathbf{F}^{(0)}:(\mathbf{F}^{(0)})^{-1}=J\delta\mathbf{F}:\mathbf{I} \tag{3}$$

Dealing with growing incompressible materials, we can make use of the multiplicative decomposition between growth and elastic deformation, introducing the following material isomorphism for the strain energy function Ψ [26]:

$$\overline{\Psi}(\mathbf{F},\mathbf{F}_g(\mathbf{X}))=(\det\mathbf{F}_g)\cdot\Psi(\mathbf{F}_e)-q(\det\mathbf{F}_e-1) \tag{4}$$

where $\mathbf{F}_e=\mathbf{F}\mathbf{F}_g^{-1}$ is a purely elastic deformation, whose incompressibility is ensured by the Lagrange multiplier q.

The nominal stress tensor for an hyperelastic continuum can be written as

$$\mathbf{S}=\frac{\partial\overline{\Psi}}{\partial\mathbf{F}}=J\mathbf{F}_g^{-1}\left(\frac{\partial\Psi}{\partial\mathbf{F}_e}-q\mathbf{F}_e^{-1}\right) \tag{5}$$

As proposed by Ben Amar and Goriely [8], considering a constant growth tensor with an incremental deformation superimposed to the actual configuration, we can define:

$$\delta\mathbf{F}_e=\delta\mathbf{F};\quad \mathbf{F}_e^{(0)}=\mathbf{F}^{(0)}\mathbf{F}_g^{-1} \tag{6}$$

so that the nominal stress tensor can be defined as $\mathbf{S}=\mathbf{S}^{(0)}+\delta\mathbf{S}^{(0)}$, where

$$\mathbf{S}^{(0)}=\left.\frac{\partial\overline{\Psi}}{\partial\mathbf{F}}\right|_{\mathbf{F}_e^{(0)}}=J\mathbf{F}_g^{-1}\left(\left.\frac{\partial\Psi}{\partial\mathbf{F}_e}\right|_{\mathbf{F}_e^{(0)}}-q(\mathbf{F}_e^{(0)})^{-1}\right) \tag{7}$$

$$\delta\mathbf{S}^{(0)}=J\mathbf{F}_g^{-1}\left(\left.\frac{\partial^2\Psi}{\partial\mathbf{F}_e\partial\mathbf{F}_e}\right|_{\mathbf{F}_e^{(0)}}:(\delta\mathbf{F}_e\mathbf{F}_e^{(0)})+q(\mathbf{F}_e^{(0)})^{-1}\delta\mathbf{F}_e-\delta q(\mathbf{F}_e^{(0)})^{-1}\right) \tag{8}$$

The incremental constitutive equation for the nominal stress can be written with respect to the actual configuration as follows:

$$\begin{aligned}\delta\mathbf{S}&=J^{-1}\mathbf{F}\delta\mathbf{S}^{(0)}=\mathbf{F}_e^{(0)}\left.\frac{\partial^2\Psi}{\partial\mathbf{F}_e\partial\mathbf{F}_e}\right|_{\mathbf{F}_e^{(0)}}:(\delta\mathbf{F}_e\mathbf{F}_e^{(0)})+q\delta\mathbf{F}_e-\delta q\mathbf{I}\\&=L:\delta\mathbf{F}_e+q\delta\mathbf{F}_e-\delta q\mathbf{I}\end{aligned} \tag{9}$$

where δq is the incremental hydrostatic pressure, and L represents the fourth-order tensor of instantaneous moduli, being the push-forward of the fixed reference elasticity tensor.

In absence of body forces, we can therefore postulate the equilibrium equation of the incremental nominal stress $\delta\mathbf{S}$ referred to the actual configuration, as follows:

$$\mathrm{div}(\delta\mathbf{S})=0 \tag{10}$$

while the incremental boundary conditions in presence of a generic traction T at a surface $\partial\Omega_l$, having unit normal $\mathbf{n}$ in the current configuration, can be written as

$$\delta\mathbf{S}^{\mathrm{T}}\mathbf{n}=T\delta\mathbf{F}^{\mathrm{T}}\mathbf{n}-\delta T\mathbf{n}\quad \text{at } \partial\Omega_l \tag{11}$$

In a general framework, incremental methods for studying plane strain instability problems in circular geometry consider a perturbation $\delta\boldsymbol{\chi}=u(r,\theta)\mathbf{e}_r+v(r,\theta)\mathbf{e}_\theta,\delta q(r,\theta)$ of the elastic solution $(\boldsymbol{\chi}_0,q)$, where $\mathbf{e}_r,\mathbf{e}_\theta$ are the unit vectors in the radial, circumferential directions. The incremental governing equations, given in Eqs. (3) and (10), read:

$$\mathrm{div}(\delta\boldsymbol{\chi})=u_{,r}+\frac{u+v_{,\theta}}{r}=0 \tag{12}$$

$$\mathrm{div}(\delta\mathbf{S})=\mathrm{div}(L:\mathrm{grad}\ \delta\boldsymbol{\chi}+q\cdot\mathrm{grad}\ \delta\boldsymbol{\chi}-\delta q\mathbf{I})=0 \tag{13}$$

where comma denotes partial derivative. Considering traction forces acting on $\partial\Omega_l$ and fixed displacements at $\partial\Omega_d$, the incremental boundary conditions read:

$$\delta\mathbf{S}^{\mathrm{T}}\mathbf{n}=T(\mathrm{grad}\ \delta\boldsymbol{\chi})^{\mathrm{T}}\mathbf{n}-\delta T\mathbf{n}\quad \text{at } \partial\Omega_l;\quad \delta\boldsymbol{\chi}=0\quad \text{at } \partial\Omega_d \tag{14}$$

The incremental stability analysis is performed looking for the three scalar functions (u,v,p) which are solution of Eqs. (12) and (13) with the boundary conditions expressed in Eq. (14). In the following, we will demonstrate how a simple canonical transform of coordinates allows to deal with the same hyperelastic problem using a fully variational method. In such a case, the elastic stability analysis will lead to the solution of a fourth-order partial differential equation of a single scalar function, which represents the generating function of a canonical transformation.

3. A variational method using the canonical transformation

The aim of this section is to define a variational formulation for studying the elastic stability of growing cylinders in plane strain conditions. First, we will introduce a general framework to define a scalar generating function of a canonical transformation. Second, we define a variational formulation of the hyperelastic problem of growing continua, demonstrating that in linear stability analysis it is equivalent to the formulation based on incremental elastic deformations.

3.1. Definitions of generating functions for incompressible deformations

In classical mechanics,[1] the canonical transformation is often employed for integrating the differential equations of motion, having the remarkable property to leave both the structure of

[1] Carathéodory [27] refers in his book that Jacobi was the first author to deal with canonical transformation, Poincaré making the first theoretical application in celestial mechanics.

Hamilton's equations and the value of the Hamiltonian function unchanged. As accurately discussed by Sewell and Roulstone [28], when dealing with planar mechanical problems a generic transformation of coordinates is canonical over a certain two-dimensional domain if it preserves the area, i.e. if the Jacobian of the transformation is equal to one. In continuum mechanics terms, a mapping $\chi : (X,Y) \rightarrow (x,y)$ is a canonical transformation if it represents an incompressible deformation. Incompressible mappings have a unique local inverse at the neighborhood of each point, but a global inverse is in general not single valued, so further restrictions on the inverse-function domain must in general be imposed. Using an isochoric mapping χ, complex function methods can be formulated to solve stability problems in finite elasticity [29]. As classically done in fluid mechanics, plane deformation problems in incremental elasticity can be simplified by the introduction of a scalar potential, which defines an infinitesimal canonical transformation of the spatial coordinates [30–32]. Although these methods allow to simplify the elastic problem accounting for a reduced number of unknown scalar functions, imposing $J=1$ everywhere avoids *a priori* the presence of elastic singularities. In Ben Amar and Ciarletta [33], we have shown that another kind of canonical transformation can be proposed for use in incompressible elasticity. In that study, we have demonstrated that accounting for internal singularities of the generating functions allows to deal with local elastic singularities in non-linear elastic problems. Extending our previous study to a generic two-dimensional elastic deformation, we remind that four different parameterizations in mixed coordinates can be proposed for defining a suitable canonical transformation:

$$Y = Y(X,y), \quad x = x(X,y) : \frac{\partial x}{\partial X} = \frac{\partial Y}{\partial y} = \frac{\partial^2 \phi_{Xy}(X,y)}{\partial X \partial y} \quad \text{if } \frac{\partial y}{\partial Y} \neq 0, \pm\infty \tag{15}$$

$$X = X(x,Y), \quad y = y(x,Y) : \frac{\partial X}{\partial x} = \frac{\partial y}{\partial X} = \frac{\partial^2 \phi_{Yx}(x,Y)}{\partial x \partial Y} \quad \text{if } \frac{\partial x}{\partial X} \neq 0, \pm\infty \tag{16}$$

$$Y = Y(X,x), \quad y = y(X,x) : \frac{\partial Y}{\partial x} = -\frac{\partial y}{\partial X} = \frac{\partial^2 \phi_{Xx}(X,x)}{\partial X \partial x} \quad \text{if } \frac{\partial x}{\partial Y} \neq 0, \pm\infty \tag{17}$$

$$X = X(Y,y), \quad x = x(Y,y) : \frac{\partial X}{\partial y} = -\frac{\partial x}{\partial Y} = \frac{\partial^2 \phi_{Yy}(Y,y)}{\partial Y \partial y} \quad \text{if } \frac{\partial y}{\partial X} \neq 0, \pm\infty \tag{18}$$

The local canonical transformations in Eqs. (15)–(18) are based on a simple application of the inverse-function theorem [34]. In Bateman [35], Eq. (17) is reported as the solution proposed by Gauss to the differential problem of finding the displacement field for an isochoric transformation. Later, Rooney and Carroll [36] extended this solution observing that, in absence of local singularities of the mixed-coordinates mapping, for each parametrization there locally exists a scalar generating function ϕ_{Ij} $(I = X,Y, j = x,y)$ which allows to put the canonical transformation in a gradient form (i.e. it represents a non-linear stream function for elastic problems). As discussed by Sewell [37] in further details, when all the four generating functions locally exist, they are connected by a closed quartet of Legendre transformations, relating the non-common arguments as the active variables. It is straightforward to show that using generating functions of a canonical transformation implies invariance not only of the Hamiltonian equations but also of the circuit integrals and the Poisson bracket operator. An extended framework for the definition of isochoric deformations in n-dimensional problems ($n > 2$) is considered in Carroll [38] and Knops [39]. In order to avoid misunderstanding, it might be useful to precise that even if in some mechanical literature canonical and contact transformation are designated as synonymous, in a general sense they are not (see [40]), as the latter are related to projective geometry and would require an additional transformation of the time coordinate in dynamical problems (e.g. wave front analysis). In the following, we will use canonical transformations in polar coordinates for defining a variational theory for hyperelastic growing tubular tissues.

3.2. A variational method for growing soft tissues with circular section

Let Ω_0 be the volume occupied by an axisymmetric soft tissue in a fixed reference configuration, and let Ω be its volume in the actual configuration. The continuous body undergoes a generic volumetric growth process, with a characteristic time considered long enough to assume separation of the growth and the visco-plastic timescales. Volumetric growth occurs under certain geometrical constraints and is subjected to traction loads acting in portions $\partial\Omega_d$ and $\partial\Omega_l$ of the actual boundary of the tissue, respectively. The description of the deformation in polar coordinates can be defined by a mapping $\chi : (R,\Theta) \rightarrow (r,\theta)$ that transforms the material point $\mathbf{R}$ to a position $\mathbf{r} = \chi(\mathbf{R})$ in the deformed configuration. As proposed by Rodriguez et al. [26], we can consider a multiplicative decomposition of growth and elastic contributions, so that we can postulate the material isomorphism for the strain energy function in Eq. (4), where $J = \det \mathbf{F}_g$ is the local volume variation due to biological growth. Soft tissues are mainly composed by water, therefore an incompressibility constraint applies to the elastic deformation $\mathbf{F}_e$. If we deal with planar strains, which is a reasonable assumption for the constrained growth problem of tubular tissues (e.g. esophagus, blood vessels, intestinal walls), the elastic deformation tensor preserves area changes, so it is tempting to apply one of the canonical transformations in Eqs. (15)–(18) to the mapping which connects the grown state to the actual configuration. In particular, considering that geometric constraints and traction loads usually apply to inner and outer radii in the reference configuration, we choose to consider a mixed coordinate parametrization with $r = r(R,\theta)$ and $\Theta = \Theta(R,\theta)$. Restricting our analysis to a homogeneous volumetric growth, we define a diagonal growth tensor $\mathbf{F}_g = \text{diag}(g_r, g_r \cdot g_\theta)$ with $g_r, g_\theta \in \Re^+$, where g_r represents an isotropic volume variation, while g_θ represents the anisotropic contribution in the circumferential direction. Recalling that $g_\theta \neq 1$ represents an incompatible grown state (not a configuration), the transformation laws of deformation in mixed polar coordinates can be expressed using the tensorial components depicted in Fig. 1.

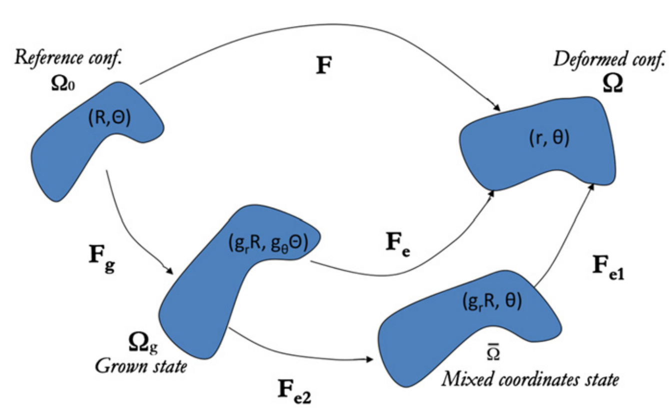

Fig. 1. Sketch of the tensorial transformations of the material isomorphism involving the growth $\mathbf{F}_g$ and the elastic deformation tensors $\mathbf{F}_e$. A mixed-coordinates state is introduced in between the intermediate grown state and the deformed configuration, using the multiplicative decomposition $\mathbf{F}_e = \mathbf{F}_{e1}\mathbf{F}_{e2}$.

In particular, a multiplicative decomposition applies to the elastic deformation tensor, so that $\mathbf{F}_e=\mathbf{F}_{e1}\mathbf{F}_{e2}$, where $\mathbf{F}_{e1}$,$\mathbf{F}_{e2}$ in components read:

$$\mathbf{F}_{e2}=\begin{bmatrix}1 & 0\\ -R\frac{\Theta_{,R}}{\Theta_{,\theta}} & \frac{1}{g_\theta\Theta_{,\theta}}\end{bmatrix};\quad \mathbf{F}_{e1}=\begin{bmatrix}\frac{r_{,R}}{g_r} & \frac{r_{,\theta}}{g_rR}\\ 0 & \frac{r}{g_rR}\end{bmatrix} \tag{19}$$

with the local restriction $\Theta_{,\theta}\neq 0,\pm\infty$ imposed by the implicit representation. From Eq. (19), the elastic deformation tensor in mixed coordinates can be written as

$$\mathbf{F}_e=\begin{bmatrix}\frac{r_{,R}}{g_r}-\frac{r_{,\theta}\Theta_{,R}}{g_r\Theta_{,\theta}} & \frac{r_{,\theta}}{g_rg_\theta R\Theta_{,\theta}}\\ -\frac{r\Theta_{,R}}{g_r\Theta_{,\theta}} & \frac{r}{g_rg_\theta R\Theta_{,\theta}}\end{bmatrix};\quad \text{with } \det\mathbf{F}_e=\frac{1}{g_r^2g_\theta}\frac{rr_{,R}}{R\Theta_\theta}=\frac{(r^2)_{,R}}{2JR\Theta_\theta} \tag{20}$$

From Eq. (22), it is interesting to look for a scalar generating function $\Phi(R,\theta)$ in order to solve exactly the incompressibility condition on $\mathbf{F}_e$. Considering a generic constant axial pre-stretch $\lambda_z>0$ on the tissue, the incompressibility constraint $\det\mathbf{F}_e\cdot\lambda_z=1$ is automatically satisfied if the mixed coordinates are implicitly expressed in the following gradient form:

$$\begin{cases} r=\sqrt{\dfrac{2\cdot\Phi_{,\theta}}{\lambda_z}}\\ \Theta=\dfrac{1}{JR}\Phi_{,R}\end{cases} \tag{21}$$

which is locally valid wherever the condition $\Phi_{,\theta R}\neq 0,\pm\infty$ holds. The coordinate transformation in Eq. (21) allows to rewrite the elastic deformation tensor in Eq. (22) as a function of the generating function $\Phi(R,\theta)$, being:

$$\mathbf{F}_e=\begin{bmatrix}\frac{1}{g_r\sqrt{2\cdot\Phi_{,\theta}\lambda_z}}\left(\Phi_{,R\theta}-\frac{\Phi_{,\theta\theta}(\Phi_{,RR}-\Phi_{,R}/R)}{\Phi_{,R\theta}}\right) & \frac{g_r}{\sqrt{2\cdot\Phi_{,\theta}\lambda_z}}\frac{\Phi_{,\theta\theta}}{\Phi_{,R\theta}}\\ -\frac{\sqrt{2\cdot\Phi_{,\theta}}}{\sqrt{\lambda_z}g_r}\frac{\Phi_{,RR}-\Phi_{,R}/R}{\Phi_{,R\theta}} & \frac{g_r\sqrt{2\cdot\Phi_{,\theta}}}{\sqrt{\lambda_z}\Phi_{,R\theta}}\end{bmatrix};$$
$$\text{with } \det\mathbf{F}_e=\frac{1}{\lambda_z} \tag{22}$$

Recalling that our boundary value hyperelastic problem can be expressed in a completely variational formulation, let us consider to different classes of boundary conditions in the following. First, if the applied body forces $\mathbf{b}$ and surface traction $\mathbf{T}$ are conservative [41], the principle of stationary potential energy Π can be written as follows:

$$\delta\Pi=\delta\Psi_{\text{int}}+\delta\Psi_{\text{ext}}=0=\delta\left(\int_{\Omega 0}[\Psi(\mathbf{R},\text{Grad }\mathbf{r})-B(\mathbf{r})]\,dV-\int_{\partial\Omega_{t0}}T(\mathbf{R},\mathbf{r})\,dA\right) \tag{23}$$

where B and T are the scalar potentials of the body and surface loads, being:

$$\mathbf{b}=\text{grad }B(\mathbf{r});\quad \mathbf{T}=\text{grad }T(\mathbf{R},\mathbf{r}) \tag{24}$$

Second, if the surface traction is only dependent on $\mathbf{R}$, which is the case of a dead loading surface traction [29] or of a live pressure loading [42], the variational problem can be expressed in a simplified form by setting $\mathbf{T}=\mathbf{PN}$, where $\mathbf{N}$ is the outer normal of the loaded surface in the reference configuration. If there exists a scalar function P such that:

$$\delta P=\text{Div }\mathbf{P}^{\mathrm{T}}\delta\mathbf{r}+\mathbf{P}^{\mathrm{T}}:\delta(\text{Grad }\mathbf{r}) \tag{25}$$

the principle of stationary potential energy can be rewritten as

$$\delta\Pi=\delta\Psi_{\text{int}}+\delta\Psi_{\text{ext}}=\delta\left(\int_{\Omega 0}[\Psi(\mathbf{R},\text{Grad }\mathbf{r})-B(\mathbf{r})-P(\mathbf{R})]\,dV\right)=0 \tag{26}$$

The hyperelastic boundary value problem is therefore equivalent to the problem of minimizing the total potential energy Π in Eq. (26), with the given constraint $\mathbf{r}=\mathbf{r}_d$ on the boundary $\partial\Omega_d$. If we transform the problem in the mixed coordinates (R,θ), the variational problem can be expressed uniquely in terms of the generating function Φ, as follows:

$$\delta\Pi(\Phi)=\delta\left(\int_{\overline{\Omega}(R,\theta)}[J\Psi(\mathbf{F}_e(\Phi_{,R},\Phi_{,\theta},\Phi_{,RR},\Phi_{,R\theta},\Phi_{,\theta\theta}))-B(\Phi_{,\theta},\theta)-P(R,\Phi_{,R})]\times\det{}^{-1}(\mathbf{F}_{e2}\mathbf{F}_g)\,d\overline{V}\right)=0 \tag{27}$$

with the displacement constraint $\mathbf{r}(\Phi_{,\theta},\Phi_{,R})=\mathbf{r}_d$ on the boundary $\partial\Omega_d$. In the following, we will derive the Euler–Lagrange equations for the variational problem expressed by Eq. (27), in order to analyze how growth can induce a bifurcation of the elastic stability in soft tubular tissues.

3.3. Euler–Lagrange equations for a growing neo-Hookean material

Let us consider the homogeneous growth of a hyperelastic hollow cylinder, indicating R_i and R_o the inner and outer radii in the reference configuration, respectively. In order to build a fully variational method, we use the canonical transformation in Eq. (21) so that the incompressibility condition for $\mathbf{F}_e$ is automatically satisfied. For the sake of simplicity, we choose a neo-Hookean constitutive equation for the material, so that the material isomorphism in Eq. (4) reads:

$$\Psi=c_1J(\mathbf{F}_e\mathbf{F}_e^{\mathrm{T}}:\mathbf{I}+\lambda_z^2-3) \tag{28}$$

where c_1 is the elastic modulus. By means of Eq. (22), the strain energy density for the incompressible body can be rewritten as

$$\Psi=c_1g_r^2g_\theta\left[\frac{1}{2g_r^2\Phi_{,\theta}\lambda_z}\left(\Phi_{,R\theta}-\frac{\Phi_{,\theta\theta}(\Phi_{,RR}-\Phi_{,R}/R)}{\Phi_{,R\theta}}\right)^2+\frac{g_r^2}{2\cdot\Phi_{,\theta}\lambda_z}\left(\frac{\Phi_{,\theta\theta}}{\Phi_{,R\theta}}\right)^2+\frac{2\Phi_{,\theta}}{\lambda_zg_r^2}\left(\frac{\Phi_{,RR}-\Phi_{,R}/R}{\Phi_{,R\theta}}\right)^2+\frac{2g_r^2\Phi_{,\theta}}{\lambda_z\Phi_{,R\theta}^2}+\lambda_z^2-3\right] \tag{29}$$

From Eq. (27), the total stationary energy per unit axial length of the growing hollow cylinder can be therefore written as

$$\Pi=\int_{R_i}^{R_o}\int_0^{2\pi}[\Psi-B(\Phi_{,\theta},\theta)-P(R,\Phi_{,R})]\frac{\Phi_{,R\theta}}{Jg_r^2}\,dR\,d\theta=\int_{R_i}^{R_o}\int_0^{2\pi}\overline{\Pi}\,dR\,d\theta \tag{30}$$

so that we can transform the boundary value problem into the Euler–Lagrange equations associated to the minimization of Π. Integrating by parts, differentiation of Eq. (30) reads:

$$\begin{aligned}\delta\Pi=&\int_{R_i}^{R_o}\int_0^{2\pi}\left[-\left(\frac{\partial\overline{\Pi}}{\partial\Phi_{,\theta}}\right)_{,\theta}-\left(\frac{\partial\overline{\Pi}}{\partial\Phi_{,R}}\right)_{,R}+\left(\frac{\partial\overline{\Pi}}{\partial\Phi_{,R\theta}}\right)_{,R\theta}+\left(\frac{\partial\overline{\Pi}}{\partial\Phi_{,\theta\theta}}\right)_{,\theta\theta}+\left(\frac{\partial\overline{\Pi}}{\partial\Phi_{,RR}}\right)_{,RR}\right]\delta\Phi\,dR\,d\theta\\&+\int_0^{2\pi}\left[\frac{\partial\overline{\Pi}}{\partial\Phi_{,R}}\delta\Phi+\frac{\partial\overline{\Pi}}{\partial\Phi_{,RR}}\delta\Phi_{,R}-\left(\frac{\partial\overline{\Pi}}{\partial\Phi_{,RR}}\right)_{,R}\delta\Phi-\left(\frac{\partial\overline{\Pi}}{\partial\Phi_{,R\theta}}\right)_{,\theta}\delta\Phi\right]_{Ri}^{Ro}d\theta\\&+\int_{Ri}^{Ro}\left[\frac{\partial\overline{\Pi}}{\partial\Phi_{,\theta}}\delta\Phi+\frac{\partial\overline{\Pi}}{\partial\Phi_{,\theta\theta}}\delta\Phi_{,\theta}-\left(\frac{\partial\overline{\Pi}}{\partial\Phi_{,\theta\theta}}\right)_{,\theta}\delta\Phi+\left(\frac{\partial\overline{\Pi}}{\partial\Phi_{,R\theta}}\right)\delta\Phi_{,\theta}\right]_0^{2\pi}dR\end{aligned} \tag{31}$$

A straightforward application of the variational method concerns the determination of an axisymmetric solution of the boundary value problem. Looking for the simple solution $\theta=\Theta$ in Eq. (21), one gets the following incompressible displacement:

$$\Phi_{,R}=JR\theta; \quad \Phi(R,\theta)=\frac{J(R^2+a)}{2}\theta \tag{32}$$

where the parameter a can be obtained by substituting the generating function given by Eq. (32) in the Euler–Lagrange equation (31), being:

$$\int_{Ri}^{Ro}\left[\frac{\partial\overline{\Pi}}{\partial\Phi_{,\theta}}-\left(\frac{\partial\overline{\Pi}}{\partial\Phi_{,R\theta}}\right)_{,R}\right]\delta\Phi\, dR=0 \tag{33}$$

Let us examine the case of particular interest where the body forces are negligible and the surface traction loads $\mathbf{T}=p(R)J\mathbf{F}^{-\mathrm{T}}\mathbf{N}$, represent a transmural pressure load $\Delta p=p(R_o)-p(R_i)$. In this case, the potential of the surface traction in Eq. (25) can be written as $P=p(R)J$, and the Euler–Lagrange equation gives

$$p(R_o)-p(R_i)=\int_{Ri}^{Ro}\left[\frac{\partial\Psi}{\partial\Phi_{,\theta}}-\left(\frac{\partial\Psi}{\partial\Phi_{,R\theta}}\right)_{,R}\right]dR=\int_{\lambda(Ri)}^{\lambda(Ro)}\frac{(\Psi)_{,\lambda}}{1-\lambda_z\lambda^2}\,d\lambda \tag{34}$$

where $\lambda=r/(Rg_\theta)$ is the principal stretch in the circumferential direction. Eq. (34) is the extension of the classical result of the inflation and extension of a circular cylindrical tube in presence of a homogeneous growth, as derived by Destrade et al. [43]. In the following we will apply the variational method developed in this section to study the growth instabilities of growing cylinders in some cases of biomechanical interest.

4. Application of the variational method for bifurcation analysis in soft tissue growth problems

In this section, we derive the Euler–Lagrange equations of the variational problem in order to investigate the bifurcation of the elastic solution. Several problems of biomechanical interests are investigated using both exact and approximated analytical techniques. We demonstrate that a perturbation of the generating function allows to explore the occurrence of complex non-linear pattern induced by growth and remodeling processes.

4.1. Euler–Lagrange equations in bifurcation analysis

If dealing with bifurcation analysis of the elastic stability, the application of the proposed variational method has several advantages compared to the method of incremental elastic deformation. In particular, the canonical transformation in mixed coordinates defines a variational problem on the scalar function $\Phi(R,\theta)$, while the incremental method requires three scalar variables, i.e. the radial and circumferential displacements and a Lagrange multiplier to impose incompressibility, which must satisfy the three governing equations Eqs. (12) and (13). Moreover, the constitutive equation for the incremental stress in Eq. (9) involves the fourth-order tensor of the instantaneous elastic moduli L, whose components in polar coordinates cannot be derived in a trivial way. In the following, we show that the two methods are equivalent in terms of linear stability analysis, while a perturbation of the generating function contains further information on the generation of asymmetric patterns in the non-linear regime.

Recalling the general axisymmetric solution in Eq. (32), let us consider a small perturbation $\phi(R,\theta)$ of the generating function Φ, as follows:

$$\Phi(R,\theta)=\frac{J}{2}(R^2+a)\Theta+\varepsilon\cdot\phi\left(\sqrt{\frac{J(R^2+a)}{\lambda_z}}\right)\cos(m\theta) \tag{35}$$

where m is a positive integer and $|\varepsilon|\ll 1$ is a small parameter. The perturbation described in Eq. (35) fulfils the incompressibility requirement exactly, while the infinitesimal scalar potentials used in incremental elasticity do it only at the infinitesimal order [30].

It is important to remark that the underlying deformation field is generally inhomogeneous, so that the perturbation of the variable R in the undeformed configuration must be done at its deformed value $r=\sqrt{J(R^2+a)/\lambda_z}$. Neglecting for the sake of notation compactness the presence of an axial pre-stretch (we set $\lambda_z=1$ everywhere in the following), the perturbation in terms of mixed variable can be expressed as

$$\begin{cases} r=\sqrt{2\cdot\Phi_{,\theta}}=\sqrt{J(R^2+a)}-\varepsilon\cdot\dfrac{\phi(\sqrt{J(R^2+a)})}{\sqrt{J(R^2+a)}}\sin(m\theta) \\ \Theta=\dfrac{1}{JR}\Phi_{,R}=\theta+\varepsilon\cdot\dfrac{\phi'(\sqrt{J(R^2+a)})}{\sqrt{J(R^2+a)}}\cos(m\theta) \end{cases} \tag{36}$$

where $'$ denotes differentiation on the argument of the scalar function. In order to represent a classical perturbation on r, let us consider $\phi(\sqrt{J(R^2+a)})=u(\sqrt{J(R^2+a)})\cdot\sqrt{J(R^2+a)}$, where u has the same physical meaning of Eq. (12), being the incremental radial perturbation. Substituting the perturbed generating function Φ expressed by Eq. (35), into the functional derivative in Eq. (31), we get at first order in ε the following Euler–Lagrange equation in the bulk medium:

$$\begin{aligned} &-(m^2-1)R^2r\left(\left(m\frac{r^2}{J}\right)^2+g_\theta^2R^2\left(3R^2-4\frac{r^2}{J}\right)\right)\cdot u(r) \\ &-r^2\left\{\left[m^2\left(-g_\theta^2R^4\left(R^2+\frac{r^2}{J}\right)+2\left(\frac{r^2}{J}\right)^3-3\left(\frac{r^2}{J}\right)^2R^2\right)\right.\right. \\ &\left.-g_\theta^2R^4\left(4\left(\frac{r^2}{J}\right)^2-3R^2\right)\right]\cdot u'(r) \\ &-R^2r\left\{\left[m^2\left(g_\theta^2R^4+\left(\frac{r^2}{J}\right)^2\right)-g_\theta^2R^2\left(8\frac{r^2}{J}-3R^2\right)\right]\cdot u''(r)\right. \\ &\left.\left.+g_\theta^2R^4r^2\left\{\left(2R^2+4\frac{r^2}{J}\right)\cdot u'''(r)+R^2r\cdot u''''(r)\right\}\right\}\right\}=0 \end{aligned} \tag{37}$$

which correspond to the fourth-order differential equation obtained by Li et al. [17] through extensive manipulation of the incremental equations of equilibrium and of incompressibility.

For what concerns boundary conditions, we must impose the extinction of the perturbation in Eq. (36) in the presence of a fixed contour $\partial\Omega_d$, so that:

$$u(r)=0; \quad u'(r)=0 \quad \text{at } \partial\Omega_d \tag{38}$$

If we deal with conservative pressure loads at the surface $\partial\Omega_l$, the boundary terms in Eq. (31) must disappear for arbitrary $\delta\Phi$ and $\delta\Phi_{,R}$, so the boundary Euler–Lagrange conditions read:

$$(m^2-1)\cdot u(r)+r\cdot u'(r)+r^2\cdot u''(r)=0 \quad \text{at } \partial\Omega_l \tag{39}$$

$$\begin{aligned} &g_\theta(m^2-1)R^2r\left(2\frac{r^2}{J}-R^2\right)\cdot u(r) \\ &+\frac{r^2}{g_\theta}\left\{\left[R^2\left(2\frac{r^2}{J}-g_\theta^2R^2\right)-m^2\left(\left(\frac{r^2}{J}\right)^2+2g_\theta^2R^4\right)\right]\cdot u'(r)\right. \\ &\left.+g_\theta^2R^2\left\{2r\left(\frac{r^2}{J}+R^2\right)\cdot u''(r)+\frac{r^2}{J}R^2\cdot u'''(r)\right\}\right\}=0 \quad \text{at } \partial\Omega_l \end{aligned} \tag{40}$$

In the next paragraphs we will apply the proposed method to study the stability of the elastic solution in some biomechanical problems of constrained growth.

4.2. Elastic instability of a growing soft ring subjected to an external pressure

Let us consider the linear stability analysis for a soft elastic ring growing under a given transmural pressure $\Delta p = p(R_o) - p(R_i)$. This situation is aimed at mimicking the long-term growth pattern of a tubular tissue expanding in a liquid-like environment (e.g. the proliferative annulus of a tumor cord in the extra-cellular matrix), where no constraints on the displacement can be imposed. In particular, we account for the presence of stress-driven remodeling forces, acting in order to optimize the distribution of the elastic strain energy inside the material. As widely studied in biomechanical literature [26,44], such remodeling processes are of utmost importance in the growth of arterial vessels. In fact, they drive the formation of an inhomogeneous transmural field of residual stresses inside the tissue, restoring an homogeneous deformation field under the external pressure. Recalling the Euler–Lagrange equation for the axisymmetric elastic solution in Eq. (34), we derive a relation between the transmural pressure and the circumferential growth g_θ needed to ensure homogeneous deformation inside the tissue:

$$p(R_o) - p(R_i) = 2c_1\left(\frac{1}{g_\theta} - g_\theta\right)\ln\left(\frac{R_o}{R_i}\right) = 2c_1\left(\frac{1}{g_\theta} - g_\theta\right)\ln\left(\frac{r_o}{r_i}\right) \tag{41}$$

as reported by Destrade et al. [43].

Under these assumptions, we can rewrite the Euler–Lagrange equation in Eq. (37) for the growing ring as follows:

$$\begin{aligned}(g_\theta^2 - m^2)(m^2-1)\cdot u(r) + r\{(m^2 + g_\theta^2(1+m^2))\cdot u'(r) + \\ + r\left[(m^2 + g_\theta^2(m^2-5))\cdot u''(r) - 6g_\theta^2 r u'''(r) - g_\theta^2 r^2 u''''(r)\right]\} = 0\end{aligned} \tag{42}$$

The solution of Eq. (48) is given by

$$\begin{aligned}u(r) = d_0\cdot\Bigg\{ & r^{\sqrt{1+\frac{m(m+g_\theta^2 m+\sqrt{8g_\theta^2(g_\theta^2+1)+m^2(g_\theta^2-1)^2})}{2g_\theta^2}}} \\ & + d_1\cdot r^{-\sqrt{1+\frac{m(m+g_\theta^2 m+\sqrt{8g_\theta^2(g_\theta^2+1)+m^2(g_\theta^2-1)^2})}{2g_\theta^2}}} \\ & + d_2\cdot r^{\sqrt{1+\frac{m(m+g_\theta^2 m-\sqrt{8g_\theta^2(g_\theta^2+1)+m^2(g_\theta^2-1)^2})}{2g_\theta^2}}} \\ & + d_3\cdot r^{-\sqrt{1+\frac{m(m+g_\theta^2 m-\sqrt{8g_\theta^2(g_\theta^2+1)+m^2(g_\theta^2-1)^2})}{2g_\theta^2}}}\Bigg\}\end{aligned} \tag{43}$$

where d_j $(j = 0,1,2,3)$ are four real constants. The boundary conditions for the fourth-order differential equation in Eq. (48) are given by the Euler–Lagrange equations in Eqs. (39) and (40), that can be simplified as:

$$(m^2-1)\cdot u(r) + r\cdot u'(r) + r^2\cdot u''(r) = 0 \quad \text{at } \partial\Omega_l : r = r_o, r_i \tag{44}$$

$$\begin{aligned}g_\theta(m^2-1)\cdot u(r) + r\{[g_\theta^2 - m^2(1+2g_\theta^2)]\cdot u'(r) \\ + 4g_\theta^2 r\cdot u''(r) + g_\theta^2 r^2\cdot u'''(r)\} = 0\end{aligned} \tag{45}$$

Considering the indetermination of d_0 for a linear stability analysis, the substitution of Eq. (43) in the four boundary relations in Eqs. (44) and (45) leads to the determination of a dispersion relation that links the circumferential growth g_θ and the instability mode m. Due to the complexity of the dispersion relation in its implicit form, we depict in Fig. 2 (left) the explicit relation between the two variables, as found with standard numerical iterative techniques. The results show that instability occurs at mode 2, as often reported for buckling phenomena under external pressure [11], and for $g_\theta > 1$, corresponding to a transmural pressure causing circumferential compression inside the tissue. Finally, the shape of the grown hollow cylinder is shown in Fig. 2 (right), showing the absence of buckling condensation phenomena typical of geometrically constrained tissues.

4.3. Instability patterns from an inhomogeneous strain field: a WKB approximation

In this paragraph, we deal with the analysis of the growth instabilities of soft cylinders subjected to a inhomogeneous deformation field. In such a case, it is not possible to find an analytical solution for the fourth-order differential Euler–Lagrange equation expressed in Eq. (37). Several numerical techniques have been established to determine the instability threshold in incremental elastic problems. In particular, a boundary value problem with two-point boundary conditions (i.e. at inner and outer radii) can be numerically integrated using displacement-traction vectors in a Stroh formulation [43]. Alternatively, a determinant method can be used

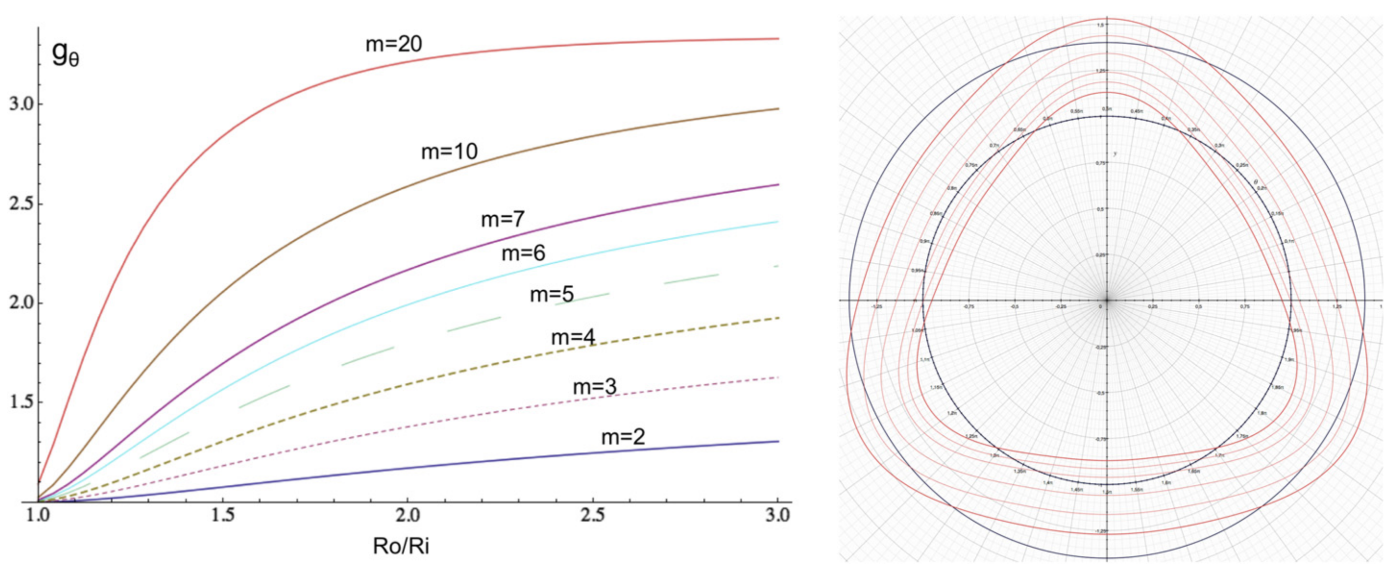

Fig. 2. Curves of marginal stability expressing the circumferential growth g_θ in function of the initial aspect ratio of the elastic tube R_o/R_i at modes m=(2,3,4,5,6,7,10,20) (left). Shape of the perturbed elastic solution at mode 3; the amplitude is set to an arbitrary value (right).

transforming the boundary value problem into an initial value problem, making use of compound matrix or impedance matrix methods to avoid numerical stiffness complications [8,45]. In the following, we will perform a WKB approximation of the perturbed elastic solution in some cases of geometrically constrained growth, demonstrating the accuracy of the approximated dispersion relation with respect to existing numerical results in biomechanical literature. Looking at the structure of the governing differential equation in Eq. (37), we observe that for $m \gg 1$ the coefficients multiplying the higher derivatives are of the order $\alpha = (1/m) \ll 1$, so a WKB approximation can be searched in the form:

$$u(r) = e^{\int_{Ro}^{R} \left(\sum_{n=1}^{\infty} \alpha^{(n-2)} u_n(s)\right) ds} \tag{46}$$

Using Eq. (46), the differential equation can be transformed into n polynomial equations in the variables u_j $(j=1,\ldots,n)$ at the order α^j. The WKB solution is analyzed for three different biomechanical problems in the following.

4.3.1. Folding of tubular tissues under geometrical constraints

Let us analyze the stability properties during the growth of an hollow cylinder subjected to a spatial confinement at a free surface. This is a case of general interest in soft tissue biomechanics, as it can represent the growth of tubular tissues when one of the constituting layers is much stiffer than the others.

For the sake of simplicity, we consider in this example only homogeneous isotropic growth (i.e. we set $g_\theta = 1$) of a one-layered material. If we impose a geometrical constraint at the outer surface, so that $r_o = R_o$, the base axisymmetric solution in Eq. (32) is given by setting $a = R_0^2(1/g_r^2 - 1)$. Recalling Eq. (46), the WKB solution at the order $n=2$ of the governing equation is given by

$$\begin{aligned} u(r) = {} & \frac{a_0 r^{-m}(r^2+(g_r^2-1)R_0^2)^{-m/2}}{\sqrt{(g_r^2-1)R_0^2(2r^2+(g_r^2-1)R_0^2)}} \cdot \{r^m(r^2+(g_r^2-1)R_0^2) \\ & + a_1 r^m (r^2+(g_r^2-1)R_0^2)^{(m+1)} + a_2 r (r^2+(g_r^2-1)R_0^2)^{(m+1)/2} \\ & + a_3 r^{(m+2)}(r^2+(g_r^2-1)R_0^2)^{(m+1)/2}\} \end{aligned} \tag{47}$$

where a_i $(i=0,\ldots,3)$ are constants to be determined. The boundary conditions for this problem are given by Eq. (38) with $\partial\Omega_d : r = r_o$, and by Eqs. (39) and (40) with $\partial\Omega_l : r = r_i$.

Given the complexity of its implicit expression, we depict in Fig. 3 (left) the solution of the boundary value problem in terms of the dispersion relation between isotropic growth g_r and the aspect ratio R_i/R_o, for several modes $m \geq 2$. Comparing to the numerical results reported in Moulton and Goriely [11], we find the same instability threshold at high instability modes, while the WKB approximation is surprisingly accurate even for low modes. The shape of the WKB solution is shown in Fig. 3 (right) setting an arbitrary finite value for the amplitude a_o. The deformed shape obtained through perturbation of the generating function in the mixed coordinates is able to capture asymmetric deformations at the inner surface, suggesting that a non-linear regime can lead to folding patterns with multiple length-scales [46].

If dealing with a spatial confinement on a the inner surface, we get $a = R_i^2(1/g_r^2 - 1)$ for the axisymmetric solution, and we find that no instability can occur, as reported by Moulton and Goriely [11]. In the next paragraph, we verify that the stability properties radically change in this problem when considering the presence of a compliant inner cylinder.

4.3.2. Surface instability of growing rings in contact with a soft core

The presence of a highly proliferative outer ring over a necrotic inner core is a common characteristic of many invasive tumors. In cylindrical geometry, this spatial confinement can lead to the occurrence of shape instabilities, as clinically observed for melanoma or tumor cords. Dervaux and Ben Amar [23] have performed experimental studies with hydrogels to mimic the growth and mass reorganization properties of soft tissues in this geometry, demonstrating that both continuous and poro-elastic theories can describe the long-wavelength instability pattern in experiments with thin growing rings.

In the following, we compare their numerical results with a WKB approximation of the elastic solution considering a homogenous isotropic growth of the outer ring. A contact surface with an inner cylinder is defined at $R = R_i$, such a soft core is not growing and its properties are indicated with subscript c in the following. The only possible elastic solution in the inner volume is given by an homogeneous deformation with $r = R$ for $R \leq R_i$. In this case, the Euler–Lagrange equation in Eq. (37) simplifies as follows:

$$\begin{aligned} & -(1-m^2)^2 \cdot u(r) + r\{(1+2m^2)\cdot u'(r) + r[(2m^2-5)\cdot u''(r) \\ & -6ru'''(r) - r^2 u''''(r)]\} = 0 \end{aligned} \tag{48}$$

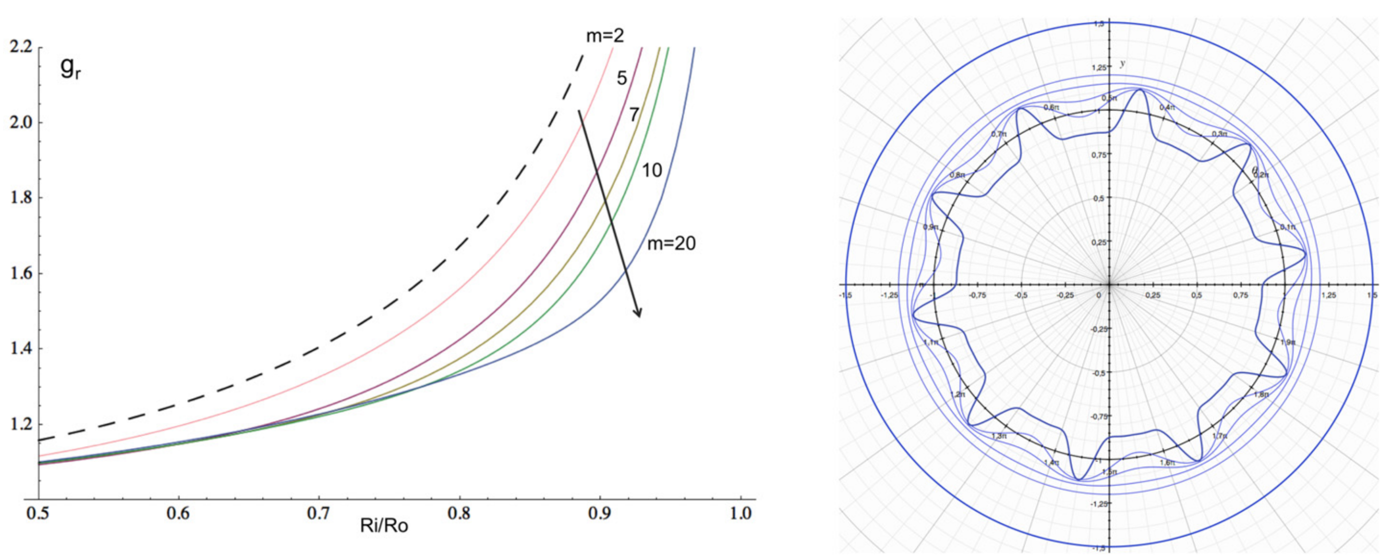

Fig. 3. Curves of marginal stability expressing the isotropic growth g_r in function of the inverse aspect ratio of the elastic tube R_i/R_o, at modes $m=2, 5, 7, 10, 20$. The dashed line represents the maximum amount of growth needed to fill the entire inner volume (left). Shape of the perturbed elastic solution at mode 10; the amplitude is set to an arbitrary finite value (right).

whose exact solution, taking care of avoiding singularities for $R=0$, is given by

$$u_c(r) = u_{c0} r^{(1-m)} + u_{c1} r^{(1+m)} \tag{49}$$

For what concerns the outer ring, the inhomogeneous deformation field in the axisymmetric base state is characterized by $a = R_i^2(1/g_r^2 - 1)$, while the WKB approximation for the perturbed state is given by Eq. (47). Six boundary conditions are needed to solve the hyperelastic problem: the two stress-free condition at the outer surface of the ring in Eqs. (39) and (40), and the four continuity equations at the inner radius of the contour integrals in Eqs. (38), (39), (40), representing continuity conditions for displacement and stress fields of the inner and the outer cylinders.

In Fig. 4, we show that, if the two bodies have the same elastic modulus, a surface instability occurs with a threshold value (evaluated at g_r about 1.495) independent on the initial thickness of the outer ring, while the first unstable mode decreases with increasing thickness. The dependence of the selected wavelength on the ratio of the elastic moduli is accurately investigated in Dervaux and Ben Amar [23], unraveling a rather complex transition in the instability pattern, characterized by a buckling condensation in the non-linear regime.

4.3.3. *Loss of circularity of a residually stressed configuration*

In this last example, we show how the residual strain field in tubular tissues can induce a bifurcation of the elastic equilibrium in the natural (unloaded) configuration. As largely discussed in biomechanical literature [13,44], anisotropic growth has a paramount importance in the morphology of tubular tissues, whose natural configuration is characterized by a cylindrical sector with an opening angle which depends on the anatomical position. If compared to classical non-linear problem for elastomers, the problem is analog to deforming a sector of a cylindrical tube into an intact annulus, whose stability in incremental elasticity has been studied by Destrade et al. [43].

Taking into account the effect of anisotropic growth in Eq. (46), the approximation at the order $n=2$ of the perturbed elastic solution is given by

$$u(r) = \frac{a_0\, r^{-m/g_\theta}(g_\theta r^2 - a)^{-m/2g_\theta^2}}{\sqrt{r^4(g_\theta^2-1) - 2ag_\theta r^2 + a^2}} \cdot \{r^{m/g_\theta}(g_\theta r^2 - a) + a_1 r (g_\theta r^2 - a)^{(1+m)/2g_\theta^2} + a_2 r^{1+2m/g_\theta}(g_\theta r^2 - a)^{(1+m)/2g_\theta^2} + a_3 r^{m/g_\theta}(g_\theta r^2 - a)^{(1+m)/g_\theta^2}\} \tag{50}$$

which is significantly different from the WKB approximation in the case of isotropic growth in Eq. (47).

In order to simplify the theoretical analysis, it is useful to remind some properties of surface instabilities in rubber materials. Since the pioneering work of Biot [47], experimental investigation indicates that a critical amount of compression can induce surface wrinkling at a free surface [48]. In cylindrical geometry, compression is known to produce creases in the inner surface of bent rubber blocks [49]. Recalling that such a surface instability is localized in a boundary layer at the inner surface, we can choose to discard the solution with positive powers of m (i.e. we set $a_2 = a_3 = 0$) and we use the simplified $u(r)$ to solve the stability problem only with respect to the two stress-free boundary conditions in Eqs. (39) and (40) at the inner radius.

In Fig. 5, the dispersion relation between g_θ and the initial aspect ratio R_o/R_i is shown at high m mode (left). The WKB solution gives the corresponding opening angle in the reference configuration (depicted in Fig. 5, right) which is in good approximation with the numerical results of Destrade et al. [43]. Not surprisingly, we get that for small thicknesses the instability threshold is given by $g_\theta \to 0$, retrieving the classical result that a thin soft plate can be bent into a closed cylinder [50].

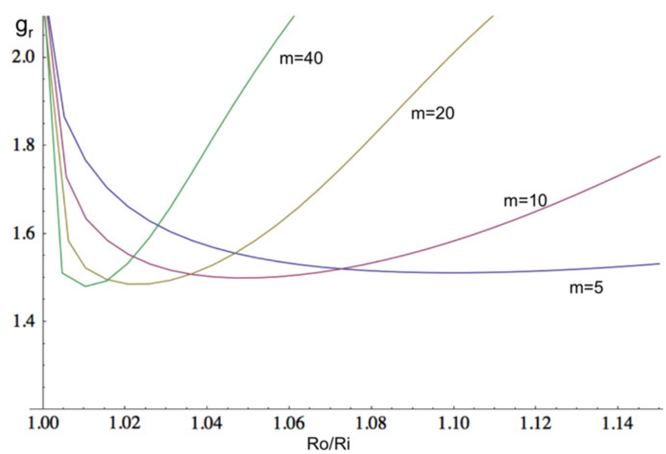

Fig. 4. Curves of marginal stability expressing the radial growth g_r in function of the initial aspect ratio of the outer ring R_o/R_i. The WKB approximation is shown at modes $m=(5,10,20,40)$, the cylinders having the same elastic modulus.

5. Discussion and conclusion

In this work, we have formulated a variational method to study the bifurcation of growing circular cylinders undergoing

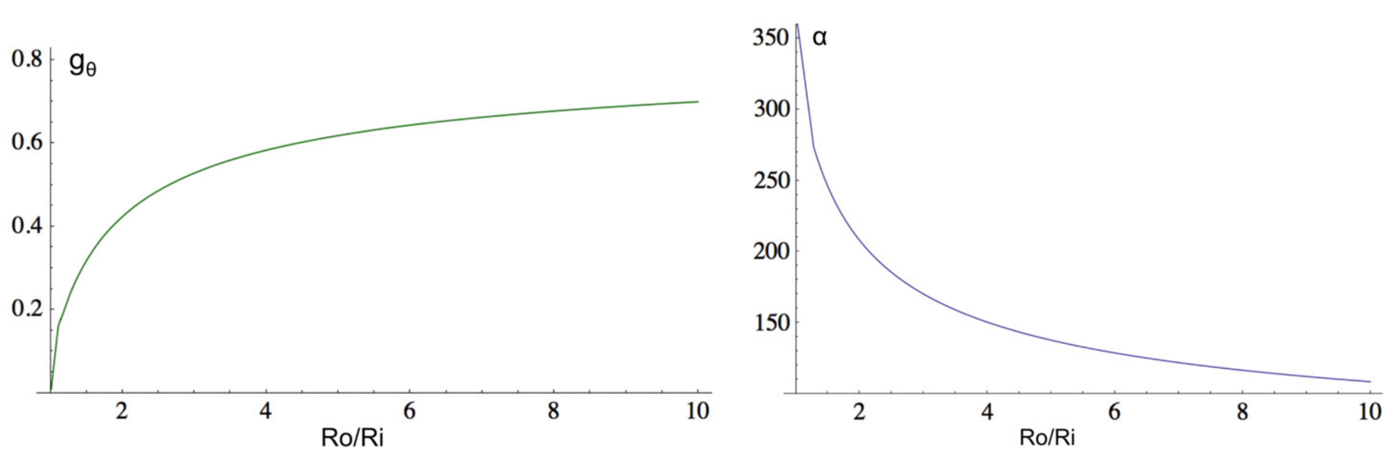

Fig. 5. Curves of marginal stability expressing the circumferential growth g_θ (left) and the opening angle $\alpha = 360(1-g_\theta)$ of the natural configuration (right), in function of the initial aspect ratio of the elastic tube R_o/R_i. The curves are shown at mode $m=50$.

conservative body forces and surface traction loads. Considering a constant axial pre-stretch, we have shown that a set of canonical transformations in mixed polar coordinates can be defined in order to provide a locally isochoric mapping of the elastic deformation. Introducing a generating function $\Phi(R,\theta)$ to derive the implicit gradient form of mixed variables (r,Θ) in Eq. (21), the incompressibility constraint on the elastic deformation tensor is solved exactly. The canonical representation has allowed to transform a generic boundary value problem dealing with conservative applied volume forces and traction into a completely variational problem. The elastic solution is given by the value of the scalar function Φ minimizing the total potential energy of the growing continuum, respecting the given boundary limitations. The Euler–Lagrange equations in the neo-Hookean case are derived in Eq. (31), while the base axisymmetric solution is given in the general case by Eqs. (32) and (34), depending on the particular boundary conditions.

The proposed variational method is applied in the bifurcation analysis of few growth problems of biomechanical interest. In a first example, we have considered the remodeling of an elastic tube, which is expanding under the external action of a transmural pressure. In such a case, remodeling forces redistribute the grown material in a anisotropic way, inducing a residual strain field which restores a homogeneous deformation in the loaded configuration. The amount of the anisotropic growth g_θ is found to depend both on the transmural pressure and on the elastic modulus of the material. We have demonstrated that a buckling instability happens for a threshold value of g_θ, increasing with the thickness of the tube and first occurring at the lowest mode $m=2$.

When perturbing an elastic solution characterized by a generally inhomogeneous deformation field, which is the typical problem of geometrically constrained growth, the Euler–Lagrange equations cannot be solved analytically. However, experimental observations report in some cases the occurrence of a surface instability confined into a boundary layer [48]. Focusing on three different examples of growth instabilities, we have shown that a WKB approximation allows to get an accurate description of the elastic solution, as validated with numerical results in biomechanical literature [11,23,43]. Interestingly, a growing ring is never unstable when fixed to an inner rigid substrate, while surface folding can happen at the free surface if the thin ring is in contact with a soft inner core. In this case, the instability threshold is lower than the one found in the case of a growing thin film attached to a planar substrate [33], and the first unstable mode is found to depend on the ring thickness.

Finally, the proposed variational method is able to provide a straightforward formulation of the linear stability analysis, which would otherwise require lengthy manipulations on the governing incremental equations. In addition, the use of a generating function allows to account for the presence of local singularities in the elastic solution. Although being out of the scopes of the present work, this feature of the variational formulation has the potential to bring insights on the non-linear treatment of instabilities. As discussed for spatially confined growth problems, i.e. constraining to a fixed external surface (see Fig. 3, right) or closing a cylindrical sector into a closed tube, the perturbed solution in mixed coordinates seems to indicate the formation of folds, possibly generating creases with multiple length-scales.

References

[1] T. Lecuit, L. LeGoff, Orchestrating size and shape during morphogenesis, Nature 450 (2007) 189–192.
[2] H.M. Zhang, C. Gally, M. Labouesse, Tissue morphogenesis: how multiple cells cooperate to generate a tissue, Curr. Opin. Cell Biol. 22 (5) (2010) 575–582.
[3] L.A. Taber, Biomechanics of growth, remodeling, and morphogenesis, Appl. Mech. Rev. 48 (1995) 487–545.
[4] L.A. Taber, Towards a unified theory for morphomechanics, Philos. Trans. R. Soc. A 367 (2009) 3555–3583.
[5] B.I. Shraiman, Mechanical feedback as a possible regulator of tissue growth, Proc. Natl. Acad. Sci. USA 102 (9) (2005) 3318–3323.
[6] P. Ciarletta, M. Ben Amar, M. Labouesse, Continuum model of epithelial morphogenesis during *C. elegans* embryonic elongation, Philos. Trans. R. Soc. A 367 (2009) 3379–3400.
[7] D. Ambrosi, L. Preziosi, G. Vitale, The insight of mixtures theory for growth and remodeling, Z. Angew. Math. Phys. 61 (2010) 177–191.
[8] M. Ben Amar, A. Goriely, Growth and instability in elastic tissues, J. Mech. Phys. Solids 53 (2005) 2284–2319.
[9] J. Dervaux, P. Ciarletta, M. Ben Amar, Morphogenesis of thin hyperelastic plates: a constitutive theory of biological growth in the Foppl-von Karman limit, J. Mech. Phys. Solids 57 (3) (2009) 458–471.
[10] P. Ciarletta, L. Foret, M. Ben Amar, The radial growth phase of malignant melanoma: multiphase modeling, numerical simulations and linear stability analysis, J. R. Soc. Interface 8 (2011) 345–368.
[11] D.E. Moulton, A. Goriely, Circumferential buckling instability of a growing cylindrical tube, J. Mech. Phys. Solids 59 (2011) 525–537.
[12] B.R. Wiggs, C.A. Hrousis, J.M. Drazen, R.D. Kamm, On the mechanism of mucosal folding in normal and asthmatic airways, J. Appl. Physiol. 83 (1997) 1814–1821.
[13] H. Gregersen, T.C. Lee, S. Chien, R. Skalak, Y.C. Fung, Strain distribution in the layered wall of the esophagus, J. Biomech. Eng. 121 (1999) 442–448.
[14] P. Ciarletta, F. Tendick, S. Micera, P. Dario, Hyperelastic model of anisotropic fiber reinforcements within intestinal walls for applications in medical robotics, Int. J. Robot. Res. 28 (10) (2009) 1279–1288.
[15] G.A. Holzapfel, R.W. Ogden, Modelling the layer-specific 3D residual stresses in arteries, with an application to the human aorta, J. R. Soc. Interface 7 (2010) 787–799.
[16] R.W. Ogden, Nonlinear elasticity, anisotropy and residual stresses in soft tissues, in: CISM Lecture Series, Springer, Wien, 2003, pp. 65–108.
[17] B. Li, Y.P. Cao, X.Q. Feng, Growth and surface folding of esophageal mucosa: a biomechanical model, J. Biomech. 44 (1) (2011) 182–188.
[18] A.E. Redington, P.H. Howarth, Airway wall remodelling in asthma, Thorax 52 (1997) 310–312.
[19] M. Ben Amar, C. Chatelain, P. Ciarletta, Contour instability in early melanoma growth, Phys. Rev. Lett. 106 (2011) 148101.
[20] J. Lowengrub, H.B. Frieboes, F. Jin, Y.-L. Chuang, X. Li, P. Macklin, S.M. Wise, V. Cristini, Nonlinear modeling of cancer: bridging the gap between cells and tumors, Nonlinearity 23 (1) R1–R91.
[21] S. Astanin, L. Preziosi, Multiphase models of tumour growth, in: N. Bellomo, M. Chaplain, E. De Angelis (Eds.), Selected Topics in Cancer Modelling: Genesis – Evolution – Immune Competition – Therapy, Birkhäuser, 2008, pp. 1–31.
[22] J. Kim, J. Yoon, R.C. Hayward, Dynamical display of biomolecular patterns through an elastic creasing instability of simuli-responsive hydrogels, Nat. Mater. 9 (2010) 159–164.
[23] J. Dervaux, M. Ben Amar, Buckling condensation in constrained growth, J. Mech. Phys. Solids 59 (2011) 538–560.
[24] D.M. Haughton, R.W. Ogden, On the incremental equations in non-linear elasticity—I. Membrane theory, J. Mech. Phys. Solids 26 (1978) 93–110.
[25] D.M. Haughton, R.W. Ogden, Bifurcation of inflated circular cylinders of elastic materials under axial loading—II. Exact theory for thick-walled tubes, J. Mech. Phys. Solids 26 (1979) 93–110.
[26] E.K. Rodriguez, A. Hoger, A. McCulloch, Stress-dependent finite growth in soft elastic tissues, J. Biomech. 27 (1994) 455–467.
[27] C. Carathéodory, Calculus of Variations and Partial Differential Equations of the First Order, third ed., AMS Chelsea, New York, 1982.
[28] M.J. Sewell, I. Roulstone, Anatomy of the canonical transformation, Philos. Trans. R. Soc. Lond. A 345 (1993) 577–598.
[29] R.W. Ogden, Non-linear Elastic Deformations, Dover, New York, 1997.
[30] M.A. Dowaikh, R.W. Ogden, On surface waves and deformations in a pre-stresses incompressible elastic solid, IMA J. Appl. Math. 44 (1990) 261–284.
[31] R.W. Ogden, Elements of theory of finite elasticity, in: Y.B. Fu, R.W. Ogden (Eds.), Non-linear Elasticity. Theory and Applications, Cambridge University Press, 2001, pp. 1–57.
[32] C.D. Coman, M. Destrade, Asymptotic results for bifurcations in pure bending of rubber blocks, Q. J. Mech. Appl. Math. 61 (2008) 395–414.
[33] M. Ben Amar, P. Ciarletta, Swelling instability of surface-attached gels as a model for soft tissue growth under geometric constraints, J. Mech. Phys. Solids 58 (2010) 935–954.
[34] U. Dini, Analisi di calcolo infinitesimale, vol. I, Nistri-Lischi, Pisa, 1907.
[35] H. Bateman, Differential Equations, Longmans, Green & Co., London, 1918.
[36] F.J. Rooney, M.M. Carroll, Generating functions for plane or axisymmetric isochoric deformations, Q. Appl. Math. 42 (1984) 249–253.
[37] M.J. Sewell, Maximum and Minimum Principle. A Unified Approach with Applications, Cambridge University Press, 1987.
[38] M.M. Carroll, A representation theorem for volume-preserving transformations, Int. J. Nonlinear Mech. 39 (2004) 219–224.
[39] R.J. Knops, On Bateman's exercise, Int. J. Nonlinear Mech. 40 (2005) 423–428.
[40] H. Goldstein, Classical Mechanics, Addison Wesley, Reading, MA, 1950.
[41] P.G. Ciarlet, Mathematical elasticity, vol. I: three-dimensional elasticity, in: Studies in Mathematics and its Applications, North-Holland, Amsterdam, 1988.
[42] P. Podio-Guidugli, A variational approach to live loadings in finite elasticity, J. Elasticity 19 (1988) 25–36.

[43] M. Destrade, J.G. Murphy, R.W. Ogden, On deforming a sector of a cylindrical tube into an intact tube: existence, unicity and stability, Int. J. Eng. Sci. 48 (2010) 1212–1224.
[44] Y.C. Fung, Biomechanics. Motion, Flow, Stress, and Growth, Springer-Verlag, New York, USA, 1990.
[45] D.M. Haughton, A. Orr, On the eversion of compressible elastic cylinders, Int. J. Solids Struct. 34 (1997) 1893–1914.
[46] F. Brau, H. Vandeparre, A. Sabbah, C. Poulard, A. Boudaoud, P. Damman, Multiple-length-scale elastic instability mimics parametric resonance of nonlinear oscillators, Nat. Phys. 7 (2011) 56–60.
[47] M.A. Biot, Surface instability of rubber in compression, Appl. Sci. Res. 12A (1963) 168–182.
[48] A.N. Gent, Elastic instabilities in rubber, Int. J. Nonlinear Mech. 40 (2005) 165–175.
[49] A.N. Gent, I.S. Cho, Surface instabilities in compressed or bent rubber blocks, Rubber Chem. Technol. 72 (1999) 253–262.
[50] D.M. Haughton, Flexure and compression of incompressible elastic plates, Int. J. Eng. Sci. 37 (1999) 1693–1708.