



MOX–Report No. 21/2011

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constitutive issues**

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# Active stress vs. active strain in mechanobiology: constitutive issues

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May 30, 2011

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## Abstract

Many biological tissues exhibit a non–standard continuum mechanics behavior: they are able to modify their placement in absence of external loads. The activity of the muscles is usually represented in solid mechanics in terms of an active stress, to be added to the standard one. A less popular approach is to introduce a multiplicative decomposition of the tensor gradient of deformation in two factors: the passive and the active one. Both approaches should satisfy due mathematical properties, namely frame indifference and ellipticity of the total stress. At the same time, the constitutive laws should reproduce the observed physiological behavior of the specific living tissue. In this paper we focus on cardiac contractility. We review some constitutive examples of active stress and active strain taken from the literature and we discuss them in terms of precise mathematical and physiological properties. These arguments naturally suggest new possible models.

**Keywords.** Active stress, active strain, rank–one convexity, cardiac mechanics, Frank–Starling law  
**MSC (2010).** 74L15, 74B20, 74E10, 74F25

## Introduction

Mechanobiology is an area of increasing interest in continuum mechanics. The impressive improvements of experimental techniques offer to scientists a huge number of data, at several spatial scales, ranging from cells to big mammals. The accuracy of experimental measures and the novelty of the observed phenomena make the mathematical modelling of biological phenomena a very attractive field. Molecular biology currently plays a major role, but there is quite a consensus that mechanics, and in particular continuum mechanics, is the correct tool for an insight of several open questions as, for instance, mechanotransduction [24].

One of the non–standard characteristics of living matter, that poses intriguing questions in continuum mechanics, is the ability of a body to change its own placement, without external loads. This property

is shared with several other mechanical systems: a few examples are thermally-induced strain in metals, swelling gels, phase transitions. In the present context the internal dynamics is due to the action of muscles, who spend energy at the microscale in order to produce a deformation at the macroscale. Our main interest is in modelling specifically the cardiac muscle, which is probably the most important example of “active biological material”. Some mathematical issues to be addressed in the paper have general validity, while the modelling aspects are dictated by our specific interest in heart physiology.

The cardiac functionality can be sketched as follows. The electric signal, produced by self-excitabile cells specifically located, starts the mechanical activity. A voltage wave then travels along the conduction fibers, depolarizes the cardiac cells, dictates the shortening of cardiomyocytes and the corresponding contraction of the cardiac muscle, that pumps the blood through the arteries and in the whole body.

The mathematical description of such a process faces a number of difficulties. Restricting to the solid mechanics issues only, the passive behavior of the cardiac wall is quite complex. The material is non-homogeneous, composed by several layers; in each layer the fibers have a specific orientation and their direction rotates for tens of degrees across the wall thickness, giving rise to a complex mechanical characterization [9]. Boundary conditions are not a trivial issue, as they are externally due to the traction exerted by other organs, while internally the blood, an incompressible fluid, prevents contraction until the valves open up. Boundary traction and elastic moduli are typically known with a severe uncertainty.

The focus of this paper is on a specific aspect involved in the mathematical modelling of active biological tissues and cardiac mechanics, in particular: we describe the heart as a continuum body and our question is how to include the active tension, due to the contraction of cardiomyocytes, in the force balance that determines its deformation. Two possible strategies are available in the literature. The most popular approach is to add an active contribution to the stress of the material [22, 18, 8, 19]. In principle, one first characterizes the passive mechanical properties of a specimen, provided that experiments are carried out in physiological conditions, and obtains a standard strain energy. Then an additive stress contribution is to be included in the force balance, typically dependent on fibre orientation, so that the observed contraction and torsion is reproduced [20].

A different point of view, inspired by the theory of active materials, has been introduced by Taber and Perucchio [25] and then deeply explored by Teresi and others [14, 5, 15]. They adopt a multiplicative decomposition of the tensor gradient of deformation, reminiscent of the theory of plasticity and, in biology, volumetric growth [21]. The deformation gradient rewrites then  $\mathbf{F} = \mathbf{F}_e \mathbf{F}_a$ , where the active contribution  $\mathbf{F}_a$  has to be constitutively provided. The active strain  $\mathbf{F}_a$  stores no energy, and it could be pictorially understood as a distortion of the microstructure, that forms a kind of watermark defined in the whole body. The elastic deformation  $\mathbf{F}_e$  must accommodate the material in order to preserve the compatibility of the deformation  $\mathbf{F}$ , possibly undermined by the distortion  $\mathbf{F}_a$ .

In this paper we examine some mathematical and biological instances of these two approaches: frame invariance, ellipticity of the stress tensor and compatibility with the expected physiological behavior. In Section 1, elementary monotonicity arguments applied to a contractile rod illustrates the very difference in the two approaches and how different models can ensure existence and uniqueness of the solution or not. In Section 2 are resumed the basic definitions of ellipticity and convexity that are to be applied to active tension models taken from the literature in Sections 4 and 5. A physiological characterization of the stress-strain curve of cardiomyocytes under pre-stretch and pressure-volume curves in the cardiac muscle are illustrated in Section 3. Conclusions and possible developments are drawn in the final section.

## 1 An elementary argument

Some elementary arguments on the active deformation of an elastic rod can turn useful to point out the essence of the active stress and active strain approaches. Consider the active stress model first. In an ide-

alized experiment, we load a one dimensional elastic rod, characterized by the homogeneous deformation  $\lambda$  and a convex strain energy  $\mathcal{W}(\lambda)$ . The balance of standard and active force reads:

$$\frac{d\mathcal{W}}{d\lambda} + \tau + \sigma = 0, \quad (1.1)$$

where  $\tau$  is the active tension,  $\sigma$  the external force. We are interested in an active tension able to produce shortening ( $\lambda < 1$ ,  $\mathcal{W}' < 0$ ), in absence of external load ( $\sigma = 0$ ), i.e.  $\tau > 0$ . For reasons to be discussed in following sections, the models presented in the literature typically assume that the active tension depends on the stretch:  $\tau = \tau(\lambda)$ . The non-trivial case we are interested in is when  $\tau|_{\lambda=1} \neq 0$  so that the relaxed state is not of equilibrium.

Eq. (1.1) provides the equilibrium strain; its existence and uniqueness are ensured if

$$\frac{d^2\mathcal{W}}{d\lambda^2} + \frac{d\tau}{d\lambda} \geq 0, \quad \forall \lambda > 0. \quad (1.2)$$

Notice that convexity of  $\mathcal{W}(\lambda)$  would be sufficient for our purposes if  $\tau$  does not depend on  $\lambda$ , but this case is not of much interest.

Depending on the specific functional forms  $\mathcal{W}(\lambda)$  and  $\tau(\lambda)$ , the condition (1.2) may be satisfied or not. Consider the following examples of active tension:

$$\tau = \kappa\lambda, \quad (1.3a)$$

$$\tau = \kappa\lambda^2, \quad (1.3b)$$

$$\tau = \kappa\lambda^{-1}, \quad (1.3c)$$

where  $\kappa > 0$ . It is an elementary calculation to check if the condition (1.2) is verified:

$$\frac{d^2\mathcal{W}}{d\lambda^2} + \kappa > 0, \quad (1.4a)$$

$$\frac{d^2\mathcal{W}}{d\lambda^2} + 2\kappa\lambda > 0, \quad (1.4b)$$

$$\frac{d^2\mathcal{W}}{d\lambda^2} - \kappa\lambda^{-2} > 0. \quad (1.4c)$$

Relations (1.4a) and (1.4b) always apply. For a given strain energy, (1.4c) reads as a restriction on the strain range that can be spanned; in particular, it might be not satisfied for large compression.

Consider the same problem illustrated above in terms of active strain: now we set  $\mathcal{W} = \mathcal{W}(\lambda/\lambda_a)$ , where  $\lambda_a$ , the active shortening, is given, and  $\tau = 0$ . The force balance equation reads

$$\frac{d\mathcal{W}}{d\lambda} \frac{1}{\lambda_a} + \sigma = 0.$$

The convexity condition at equilibrium state is:

$$\frac{d^2\mathcal{W}}{d\lambda^2} \frac{1}{\lambda_a^2} > 0.$$

In this case, existence and uniqueness of equilibrium are ensured by the mere convexity of the strain energy function.

The elementary argument sketched above illustrates the motivation of this paper: to point out the mathematical properties and physiological characteristics that a model for active contraction should possess and possibly propose new approaches that fulfill such requirements.

## 2 Introductory notions

The motion of a continuum body is an invertible smooth map from an open set of  $\mathbb{R}^3$  into  $\mathbb{R}^3$ ; the function  $\mathbf{x} = \mathbf{x}(\mathbf{X}, t)$  associates every point  $\mathbf{X}$  in the initial (relaxed) configuration to its current placement  $\mathbf{x}$ . The gradient of this function is a tensor (the tensor gradient of deformation):

$$\mathbf{F} = \text{Grad } \mathbf{x}, \quad F_{ij} = \frac{\partial x_i}{\partial X_j}, \quad 1 \leq i, j \leq 3.$$

The tensor gradient of deformation belongs to the space on linear operators with strictly positive determinant  $\mathbb{L}\text{in}^+$ .

The tensional state in an elastic homogeneous continuum medium is described in material coordinates by the Piola stress tensor  $\mathbf{P}(\mathbf{F})$ . The following definitions hold:

$$\mathbf{P} = J\mathbf{T}\mathbf{F}^{-T}, \quad \mathbf{S} = J\mathbf{F}^{-1}\mathbf{T}\mathbf{F}^{-T} = \mathbf{F}^{-1}\mathbf{P},$$

where  $\mathbf{T}$  is the Cauchy stress tensor,  $\mathbf{S}$  is the second Piola stress tensor and  $J = \det(\mathbf{F})$ . For an hyperelastic material, it exists a strain energy function  $\mathscr{W} : \mathbb{L}\text{in}^+ \rightarrow \mathbb{R}$  such that

$$\mathbf{P} = \frac{\partial \mathscr{W}}{\partial \mathbf{F}}, \quad (2.1)$$

where the symbol at the right hand side denotes the Fréchet derivative.

The strain energy of soft biological tissues typically depends on the orientation and elongation of fibers of different nature. Denoting by  $\mathbf{n}(\mathbf{X})$ , the (unique) orientation of the fibers in the point  $\mathbf{X}$  of the body in its referential configuration, we have  $\mathscr{W} = \mathscr{W}(\mathbf{F}; \mathbf{n})$ , where the dependence of the strain energy on  $\mathbf{n}$  is of parametric nature [12]. For the sake of simplicity, we omit to indicate explicitly such a dependence in the following, but the results illustrated in the present work remain valid in the general anisotropic case. In particular, if the strain energy function is invariant with respect to rotations of the form  $\mathbf{n} \otimes \mathbf{n}$ , then it depends on  $\mathbf{n}$  only through a set of scalar quantities like<sup>1</sup>  $I_4 = \mathbf{F}\mathbf{n} \cdot \mathbf{F}\mathbf{n}$  and  $I_5 = \mathbf{F}^{-T}\mathbf{n} \cdot \mathbf{F}^{-T}\mathbf{n}$  [11].

The constitutive relation for an elastic material  $\mathbf{P} = \mathbf{P}(\mathbf{F})$  is strictly monotone if

$$\left( \mathbf{P}(\mathbf{F} + \alpha\mathbf{H}) - \mathbf{P}(\mathbf{F}) \right) : \mathbf{H} > 0, \quad \text{for each } \mathbf{F} \in \mathbb{L}\text{in}^+, \mathbf{H} \neq 0 \text{ and } \alpha \in (0, 1] \text{ such that } \det(\mathbf{F} + \alpha\mathbf{H}) > 0. \quad (2.2)$$

In case of hyperelastic material, the definition (2.2) corresponds to the strict convexity of the strain energy function:

$$\alpha\mathscr{W}(\mathbf{F}) + (1 - \alpha)\mathscr{W}(\mathbf{F} + \mathbf{H}) > \mathscr{W}(\mathbf{F} + (1 - \alpha)\mathbf{H}), \quad \text{for each } \mathbf{F} \in \mathbb{L}\text{in}^+, \mathbf{H} \neq 0 \text{ and } \alpha \in (0, 1) \text{ such that } \det(\mathbf{F} + (1 - \alpha)\mathbf{H}) > 0. \quad (2.3)$$

If  $\mathbf{P}(\mathbf{F})$  is differentiable, the condition (2.2) is equivalent to say that the second derivative of the energy is a positive definite linear operator (cfr. (2.1)):

$$\mathbf{H} : \frac{\partial \mathbf{P}(\mathbf{F})}{\partial \mathbf{F}} : \mathbf{H} > 0, \quad \text{for each } \mathbf{F} \in \mathbb{L}\text{in}^+ \text{ and } \mathbf{H} \neq 0. \quad (2.4)$$

Despite its appeal, strict monotonicity is a too restrictive condition for several reasons [2]. A well established weaker characterization is the strong ellipticity condition: inequality (2.4) must hold for any

<sup>1</sup>We use standard enumeration for these invariants.

increment  $\mathbf{H}$  of rank–one. Analogously, a strain energy is rank–one convex if (2.4) holds for any increment  $\mathbf{H}$  of rank–one. Notice that the set of the rank–one tensors is represented by the dyads  $\mathbf{a} \otimes \mathbf{b}$  where  $\mathbf{a}, \mathbf{b} \in \mathbb{R}^3$ .

Finally, if the material is incompressible, the condition  $\det(\mathbf{F} + \alpha\mathbf{H}) = 1$  should be added in (2.2) and, for a smooth enough strain energy function, this condition translates into  $\mathbf{F}^{-T} : \mathbf{H} = 0$  in inequality (2.4). If the increment is a rank–one tensor, i.e.  $\mathbf{H} = \mathbf{a} \otimes \mathbf{b}$ , then it must be  $\mathbf{F}^{-T} : \mathbf{H} = \mathbf{a} \cdot \mathbf{F}^{-1}\mathbf{b} = 0$ .

### 3 Physiological facts

While the mathematical results illustrated in the next sections may apply to any active material, the modelling issues refer to the specific problem that we have in mind, namely the heart contraction. A milestone of the physiological literature in this respect is that a mathematical model designed to predict the solid mechanics behavior of the cardiac muscle should be able to reproduce the active tension according to the Frank–Starling law. Its qualitative statement is the following: “the greater the volume of blood entering the heart during diastole (end–diastolic volume), the greater the volume of blood ejected during systolic contraction (stroke volume) and vice-versa”. In dynamic terms, this means that the larger the passive strain of the cardiac muscle originated by the venous pressure before contraction, the larger the active stress. This relation has a clear functional motivation: the muscle applies a bigger force when a greater work has to be performed, thus pumping a larger volume of blood.

This self–regulation mechanism at a tissue level has a striking counterpart at a cellular level, where a quantitative evidence is offered by several experiments. Cardiomyocytes stretched up to 1.3 times of their original length apply an active force, after electric stimulus, that grows linearly with the pre–stretch [10]. This relation is apparent in the plot of Figure 1 (a sketch of the results reported by Iribe et al. [10]). A

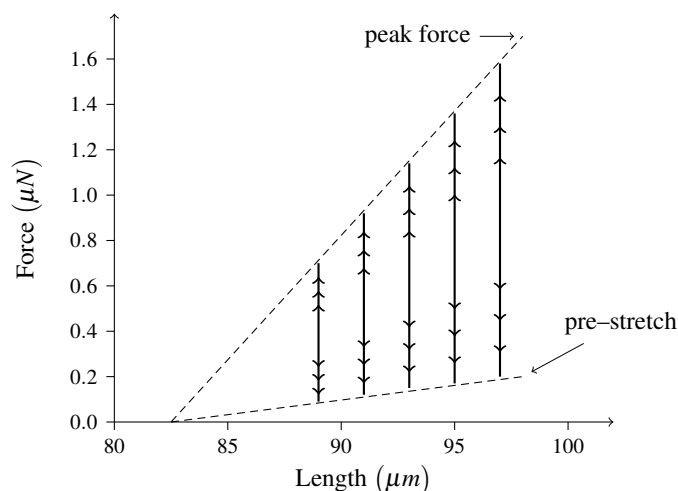


Figure 1: Cardiomyocytes electrically stimulated under isometric conditions: the produced force grows linearly with the pre–stretch [sketch from Figure 5A of [10]].

cardiomyocyte undergoes isometric contractions after pre–stretch at different ratios (lower straight line). The cell is activated by a voltage difference while kept at a constant length. The produced force depends linearly on the pre–stretch (difference between the value of the two lines) at fixed length.

While the active–passive stress–strain relations are well understood at a cellular level, to our knowledge a quantitative Frank–Starling law at a tissue scale has not been stated yet. The prototypical setup to state a force–strain relation at the macroscale is the pressure–volume curve that occurs in the heart during its cycle. Figure 2 shows the different pressure–volume loops that can be obtained in a ventricle by tuning

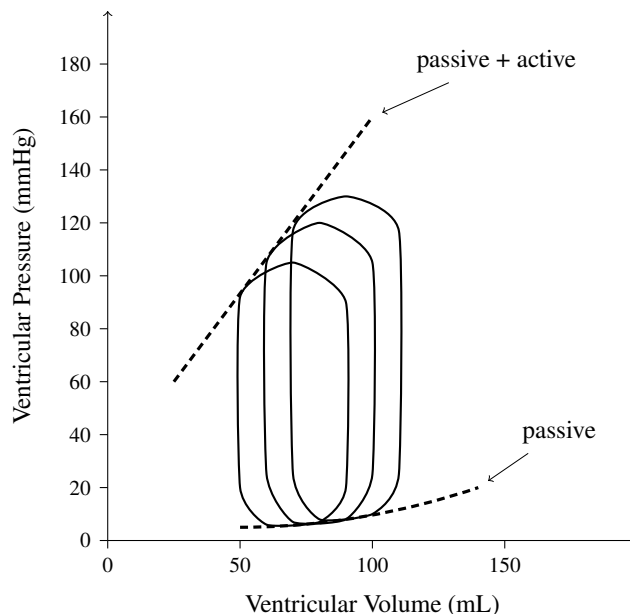


Figure 2: Pressure–volume loops in a ventricle allow to determine the curve of the passive and active normal stress at the cardiac wall [sketch from Figure 12 of [7]].

the aortic pressure. This plot provides the quantitative dependence of the active stress on the deformation [4, 15]: the upper and lower dashed lines denote the pressure of the fluid, i.e. the radial stress at the inner wall, both when the stress is purely passive (lower curve) and when the stress is actively produced (upper curve).

In this paper we do not enter further physiological details and the reader interested in cardiac physiology may refer to the cited literature. We just point out that it is not trivial to match the cellular and tissutal experiments in order to state a macroscopic constitutive equation. At the macroscale, the curves reported in the literature clearly show a strongly nonlinear dependence of the active stress (measured by the pressure of the fluid) and the strain (represented by the change in volume). In fact, the hoop stress in a hollow elastic sphere filled by a fluid at pressure  $p$  obeys the Laplace formula:

$$T_{\Theta\Theta} = \frac{rp}{2h},$$

where  $r$  is the radius,  $h$  the thickness of the wall and  $T_{\Theta\Theta}$  is an averaged hoop stress (basically the active stress, in our case). For an incompressible material, the constant volume of the solid body is  $\simeq r^2h$  and therefore, as a rule of thumb,

$$T_{\Theta\Theta} = \frac{rp}{2h} \simeq r^3p \simeq r^6, \quad (3.1)$$

where the dependence of the pressure on the volume has been exported by the curve in Figure 1. As the hoop strain is proportional to  $r$ , it follows from (3.1) that the active stress grows very nonlinearly with the deformation. Quoting Downey: “increasing end–diastolic volume actually diminishes the heart’s



ability to convert its fiber tension into pressure. In the physiological range, this disadvantage is greatly overshadowed by the increase in force generation that results from the longer fiber length". As a matter of fact, Teresi and coworkers reproduce the plot of Figure 2 in an active strain framework choosing a constitutive law for the stress that grows with the sixth power of the strain [15].

We close this section mentioning that active stress models reported in the literature are sometimes inspired by experimental evidence at a cell-scale, sometimes they account for a macroscopic behavior directly. The first approach is clearly more satisfactory from a methodological point of view and the efficacy of the active constitutive relation at a tissue scale is to be verified *a posteriori*, typically on the basis of numerical simulations.

## 4 Active stress

We address first the question whether ellipticity of the Piola stress tensor is ensured when adopting an active stress approach. The aim is to investigate the mathematical characteristics of the equilibrium predicted by models currently adopted in numerical codes, as well as to discuss their physiological basis.

In general there is no reason why the active stress tensor should arise from a potential, and in fact it is not a conservative force. We therefore investigate ellipticity by direct derivation of the total stress. If now  $\mathcal{W} = \mathcal{W}(\mathbf{F})$ , the total Piola stress reads

$$\mathbf{P} = \frac{\partial \mathcal{W}}{\partial \mathbf{F}} + \mathbf{P}_a$$

where  $\mathbf{P}_a = \mathbf{F}\mathbf{S}_a$  is the active Piola stress to be prescribed, possibly depending on  $\mathbf{F}$ .

If the material is hyperelastic in its passive mechanical behavior, the condition (2.4) rewrites now

$$\mathbf{H} : \frac{\partial^2 \mathcal{W}}{\partial \mathbf{F} \partial \mathbf{F}} : \mathbf{H} + \mathbf{H} : \frac{\partial \mathbf{P}_a}{\partial \mathbf{F}} : \mathbf{H} > 0, \quad \forall \mathbf{F} \in \mathbb{L}\text{in}^+, \mathbf{H} \neq 0, \quad (4.1)$$

with the additional constraint  $\mathbf{F}^{-T} : \mathbf{H} = 0$  in the case of incompressible material.

Given for granted that  $\mathcal{W} = \mathcal{W}(\mathbf{F})$  is a rank-one convex function, inequality (4.1) reads as a condition on the functional form of the active stress. In this section we address the ellipticity of the total stress  $\mathbf{P}$  by checking the positivity of the second term at the right hand side of (4.1) for some specific models taken from the literature. If the active term in (4.1) is not positive, the inequality can still hold, depending on the specific strain energy  $\mathcal{W}(\mathbf{F})$ , but conditions can apply on the admissible strain range.

Notice that possible strong mathematical properties of the active stress  $\mathbf{P}_a$  (as strict monotonicity) are not to be deprecated, because the sum of two functions retains the (good) properties of the weaker one. Conversely, if  $\mathbf{P}_a$  is not at least rank-one elliptic, the existence of the solution might be not ensured.

### 4.1 Examples from the literature

One possible form of the active tension that does not involve an active role for the fibers is proposed by Panfilov et al. [18] in terms of second Piola–Kirchhoff active stress tensor:

$$\mathbf{S}_a = \tilde{\mathcal{S}}_a \mathbf{C}^{-1} \quad (4.2)$$

where  $\mathbf{C} = \mathbf{F}^T \mathbf{F}$ . In an electromechanical model, the scalar quantity  $\tilde{\mathcal{S}}_a$  depends on the activated state of the material, possibly thanks a delay equation; however such a dependence is not of interest herein,

where balance of forces applies in static form, and we take it constant. Notice that the Cauchy stress corresponding to (4.2) is spherical. Here the first Piola stress reads

$$\mathbf{P} = \frac{\partial \mathcal{W}}{\partial \mathbf{F}} + \tilde{S}_a \mathbf{F}^{-T},$$

where  $\mathcal{W}$  is a strain energy of a compressible material. The ellipticity can be checked by further derivation:

$$\mathbf{H} : \frac{\partial^2 \mathcal{W}}{\partial \mathbf{F} \partial \mathbf{F}} : \mathbf{H} - \tilde{S}_a \mathbf{F}^{-T} \mathbf{H}^T \mathbf{F}^{-T} : \mathbf{H} > 0. \quad (4.3)$$

The last term at the right hand side can be negative (take, for instance,  $\mathbf{H} = \mathbf{a} \otimes \mathbf{a}$ ) and, depending on the specific form of the strain energy, the total stress might not be unconditionally strongly elliptic. In particular the condition (4.3) may be not satisfied for large compressions.

A constitutive equation for active stress that accounts for the orientation of the fibers can be written in a general form as follows:

$$\mathbf{P}_a = S_a(I_4) \mathbf{F} \mathbf{n} \otimes \mathbf{n} \quad (4.4)$$

where  $S_a$  is a positive function of  $I_4 = \mathbf{F} \mathbf{n} \cdot \mathbf{F} \mathbf{n}$  (in the range of interest). A popular choice, firstly proposed by Smith et al. [22] and then adopted by other groups, is a dependence of the following type:

$$S_a(I_4) = \tilde{S}_a \frac{1 + \beta (\sqrt{I_4} - 1)}{I_4}, \quad (4.5)$$

where  $\beta$  and  $\tilde{S}_a$  are constant in this context and the active stress works only when the fibers are elongated ( $I_4 > 1$ ). The numerator of the r.h.s. term encodes the Frank–Starling effect while the denominator can be interpreted as a normalization factor accounting that  $S_a$  is a Cauchy stress per unit fiber length.

Böl et al. [3] propose

$$S_a(I_4) = f_0 + \tilde{S}_a \left( 1 - e^{-\eta(\sqrt{I_4} - 1)} \right), \quad (4.6)$$

which accounts for the Frank–Starling effect directly at a macroscopic level.

Finally Pathmanathan et al. [19] adopt a form of the active stress tensor that can be obtained deriving a scalar function:

$$\mathbf{P}_a = \tilde{S}_a \frac{\partial}{\partial \mathbf{F}} (\log(\mathbf{F} \mathbf{n} \cdot \mathbf{F} \mathbf{n})) = 2 \frac{\tilde{S}_a}{I_4} \mathbf{F} \mathbf{n} \otimes \mathbf{n}. \quad (4.7)$$

Such a scalar function should not be understood as a strain energy, as no conservation applies: the possibility to derive the stress from a scalar is just a technical tool that simplifies the analysis. As a matter of fact, the Piola stress (4.7) is not even rank–one elliptic and therefore, for a given generic passive strain function, strong ellipticity of the total stress holds under condition.

Irrespective of the specific form at hand, the strong ellipticity of the active stress forms illustrated above can be checked by direct derivation of (4.4). In fact, strong ellipticity for a given deformation  $\mathbf{F}_0$ , with  $\mathbf{H} = \mathbf{a} \otimes \mathbf{b}$  reads as follow:

$$\mathbf{H} : \frac{\partial \mathbf{P}_a}{\partial \mathbf{F}} \Big|_{\mathbf{F}_0} : \mathbf{H} = \left[ 2S'(\mathbf{F}_0 \mathbf{n} \cdot \mathbf{a})^2 + S(\mathbf{a} \cdot \mathbf{a}) \right] (\mathbf{b} \cdot \mathbf{n})^2 \geq 0, \quad (4.8)$$

and here we denote

$$S = S_a \Big|_{\mathbf{F}_0}, \quad S' = \frac{dS_a}{dI_4} \Big|_{\mathbf{F}_0}.$$

The condition  $\mathbf{F}_0^{-1} \mathbf{a} \cdot \mathbf{b} = 0$  on the admissible virtual displacements dictated by the incompressibility constraint is accomplished taking  $\mathbf{a} = \mathbf{F}_0 \mathbf{m}$ , with  $\mathbf{m}$  such that  $\mathbf{m} \cdot \mathbf{b} = 0$ .

We start observing that strict inequality is not satisfied in (4.8) if  $\mathbf{b} \cdot \mathbf{n} = 0$ . In the other cases the last factor can be dropped and the following condition remains:

$$2S'(\mathbf{F}_0 \mathbf{n} \cdot \mathbf{a})^2 + S(\mathbf{a} \cdot \mathbf{a}) \geq 0. \quad (4.9)$$

If  $S_a(I_4)$  is a monotone increasing function of its argument, the inequality (4.9) is always verified. Conversely, if  $S_a(I_4)$  is a monotone decreasing function, by application of the Cauchy-Schwarz inequality,

$$2S'(\mathbf{F}_0 \mathbf{n} \cdot \mathbf{a})^2 + S(\mathbf{a} \cdot \mathbf{a}) \geq 2S'(\mathbf{F}_0 \mathbf{n} \cdot \mathbf{F}_0 \mathbf{n})(\mathbf{a} \cdot \mathbf{a}) + S(\mathbf{a} \cdot \mathbf{a}),$$

we can state the following sufficient condition for the rank–one ellipticity of active stress tensors of the form (4.4):

$$2S'(\mathbf{F}_0 \mathbf{n} \cdot \mathbf{F}_0 \mathbf{n}) + S \geq 0.$$

**Remark** If an active stress model is not rank–one elliptic, an equilibrium solution of the force balance equation may not exist, at least for some range of the strain. In the numerical approximation of the momentum equation, the absence of equilibrium configurations might be interpreted as a numerical instability to be addressed by a more careful numerical discretization. However, no numerical strategy can cure an ellipticity loss of the differential equations.

## 4.2 A physiologically motivated active stress

In this section we introduce an active stress form that satisfies rank–one ellipticity, frame indifference and, for infinitesimal strains of for homogeneous deformations along the direction of the fibers  $\mathbf{n}$ , accommodates the Frank–Starling law in its cell–scale version. Consider

$$\mathbf{T} = \frac{1}{J} \frac{\partial \mathcal{W}}{\partial \mathbf{F}} \mathbf{F}^T + \frac{S_a}{J} \frac{\mathbf{F} \mathbf{n} \otimes \mathbf{F} \mathbf{n}}{\sqrt{I_4}},$$

and, in terms of Piola stress,

$$\mathbf{P} = \frac{\partial \mathcal{W}}{\partial \mathbf{F}} + S_a \frac{\mathbf{F} \mathbf{n} \otimes \mathbf{n}}{\sqrt{I_4}}. \quad (4.10)$$

The active component of the Piola tensor (4.10) is a strictly monotone linear operator. A simple way to prove it is to notice that such a specific constitutive form can be obtained by derivation of scalar function

$$\mathcal{W}_a = S_a \sqrt{I_4}.$$

As  $\mathcal{W}_a$  is convex, the corresponding active stress tensor is monotone. In fact the inequality

$$\alpha \mathcal{W}_a(\mathbf{F}) + (1 - \alpha) \mathcal{W}_a(\mathbf{G}) \geq \mathcal{W}_a(\alpha \mathbf{F} + (1 - \alpha) \mathbf{G}),$$

for each  $\mathbf{F}, \mathbf{G} \in \mathbb{L}in^+$  and  $\alpha \in (0, 1)$  such that  $\det(\alpha \mathbf{F} + (1 - \alpha) \mathbf{G}) > 0$ .

follows from

$$|\mathbf{F} \mathbf{n}| |\mathbf{G} \mathbf{n}| \geq |\mathbf{F} \mathbf{n} \cdot \mathbf{G} \mathbf{n}|.$$

Notice that the sum of two functions retains the regularity properties of the less regular one; in our case strict rank–one convexity of  $\mathcal{W}$  and convexity of  $\mathcal{W}_a$  ensure strict rank–one convexity of  $\mathcal{W} + \mathcal{W}_a$ .

### 4.3 Boundary conditions

The active stress is originated by fiber contraction, their orientation being  $\mathbf{n}$  in the reference configuration and  $\mathbf{F}\mathbf{n}$  in the current one. As the fibers are tangential to the surface at the boundary, a reasonable requirement is that they do not contribute to the traction balance at the boundary itself, i.e.

$$\mathbf{P}_a \mathbf{m} = 0,$$

where  $\mathbf{m}$  is the normal to the boundary in the reference configuration. The reader can notice that such a characterization is satisfied by the active stress tensors (4.4) and (4.10).

## 5 Active strain

Consider now a modified convex energy of the form  $\mathscr{W} = \mathscr{W}(\mathbf{F}_e)$ , where  $\mathbf{F} = \mathbf{F}_e \mathbf{F}_a$ . The meaning of this assumption is as follows: in absence of external forces the minimum of energy (the relaxed configuration) is shifted by the internal active forces to the configuration  $\mathbf{F} = \mathbf{F}_a^{-1}$  and no energy is stored by the action of the internal active forces [6]. The corresponding Piola stress, evaluated in the reference configuration, is obtained by a pull back of the Frechet derivative of the strain energy:

$$\mathbf{P}(\mathbf{F}) = \det(\mathbf{F}_a) \frac{\partial \mathscr{W}}{\partial \mathbf{F}_e} \mathbf{F}_a^{-T}.$$

We start checking if convexity is preserved. The answer is positive:  $\forall \mathbf{H} \neq 0$  it holds

$$\mathbf{H} : \frac{\partial^2 \mathscr{W}}{\partial \mathbf{F} \partial \mathbf{F}} : \mathbf{H} = \mathbf{H} : \left( \frac{\partial^2}{\partial \mathbf{F} \partial \mathbf{F}} \mathscr{W}(\mathbf{F} \mathbf{F}_a^{-1}) \right) : \mathbf{H} = \mathbf{H} \mathbf{F}_a^{-1} : \frac{\partial^2 \mathscr{W}}{\partial \mathbf{F} \partial \mathbf{F}} : \mathbf{H} \mathbf{F}_a^{-1} > 0.$$

Rank-one convexity is granted by the properties of  $\mathscr{W}$ ; in fact if  $\mathbf{H}$  is a rank-one tensor, also  $\mathbf{H} \mathbf{F}_a^{-1}$  is a rank-one tensor.

For a frame invariant strain energy, here the principle of material indifference for change in observer is abided if the gradient of deformation in its factorial representation transforms correctly:

$$\mathbf{F}^* = \mathbf{Q} \mathbf{F} \quad \Rightarrow \quad \mathbf{F}_e^* \mathbf{F}_a^* = \mathbf{Q} \mathbf{F}_e \mathbf{F}_a,$$

for any rotation  $\mathbf{Q}$ . The simplest way to obey this prescription is to choose  $\mathbf{F}_a$  invariant:  $\mathbf{F}_a^* = \mathbf{F}_a$ . It follows that

$$\mathbf{F}_e^* = \mathbf{F}^* (\mathbf{F}_a^*)^{-1} = \mathbf{Q} \mathbf{F} (\mathbf{F}_a)^{-1} = \mathbf{Q} \mathbf{F}_e.$$

The Cauchy stress is,

$$\mathbf{T} = \mathbf{P} \mathbf{F}^T = \frac{\partial \mathscr{W}}{\partial \mathbf{F}} \mathbf{F}^T = (\det \mathbf{F}_a) \mathscr{W}' \mathbf{F}_a^{-T} \mathbf{F}^T \quad (5.1)$$

where  $\mathscr{W}'$  denotes differentiation of  $\mathscr{W}$  with respect to its argument.

Since, in general, there are no apparent passive and active stress herein, it is not immediate to argue the physiological admissibility of the model in terms of ‘‘Cauchy stress growing with strain’’, along the same lines exposed in the previous sections. However specific constitutive forms allow to outline an analogy.

A frame invariant constitutive equation for the active strain  $\mathbf{F}_a$  that naturally accounts for the contraction of the fibers is

$$\mathbf{F}_a = \mathbf{1} - \gamma \mathbf{n} \otimes \mathbf{n},$$

where  $\gamma$  is a positive constant,  $1 > \gamma > 0$ , and  $\mathbf{1}$  is the identity tensor. The determinant and the inverse of  $\mathbf{F}_a$  can be explicitly calculated (see Appendix A)

$$\det(\mathbf{F}_a) = 1 - \gamma, \quad \mathbf{F}_a^{-1} = \mathbf{1} + \frac{\gamma}{1 - \gamma} \mathbf{n} \otimes \mathbf{n}.$$

Let us suppose that the strain energy of the inert material be the sum of a neo-Hookean isotropic contribution plus a transverse isotropic one, as follows:

$$\mathcal{W}(\mathbf{F}_e) = \frac{\mu_1}{2} \mathbf{F}_e : \mathbf{F}_e + \frac{\mu_2}{2} \mathbf{F}_e \mathbf{n} \cdot \mathbf{F}_e \mathbf{n}.$$

According to (5.1), the corresponding Cauchy (total) stress is<sup>2</sup> (see Appendix B)

$$\mathbf{T} = \mu_1 \left( \mathbf{F}\mathbf{F}^T - \gamma \mathbf{F}\mathbf{F}^T + \gamma \frac{2 - \gamma}{1 - \gamma} \mathbf{F}\mathbf{n} \otimes \mathbf{F}\mathbf{n} \right) + \mu_2 \left( 1 + \frac{\gamma}{1 - \gamma} \right) \mathbf{F}\mathbf{n} \otimes \mathbf{F}\mathbf{n}. \quad (5.2)$$

The polynomial strain energy allows here to recover an interpretation of the active strain in terms of active stress. We devise in (5.2) a standard passive Cauchy stress plus an extra one: all the terms depending on  $\gamma$  can be understood as active dynamic contribution. The same comment would not apply for a non-polynomial energy and, as a matter of fact, exponential strain energies are common in biomechanics. Notice that all the active contributions (5.2) are quadratic in the deformation, a direct consequence of the quadratic form of the neo-Hookean Cauchy stress.

## Final remarks

In this paper we have addressed the correct mathematical statement of the contractility of a muscle, with a focus on the cardiac system. While the mathematical results have a general validity, the physiological characterization pertains the specific system at hand.

An acceptable mathematical model for the active behavior of the cardiac muscle should satisfy mathematical and biological requirements.

- Correct biological behavior: when the effective potential wave activates the muscle, the material should contract in the direction of the fibers. It is experimentally observed that the cardiac wall produces an active stress that grows with the stretch. The dependence between stretch and active stress is linear at a cell level, typically nonlinear at a tissue level, an issue that remains to be better understood.
- The total stress must obey frame invariance and a suitable sign preserving condition (rank-one ellipticity, in the present work).

A constitutive form of the active stress should be prescribed with the due attention to the properties listed above. If the active stress in itself is not at least rank-one elliptic, a condition on the ellipticity of the total stress can arise, typically limiting the maximum admissible strain [19]. On the other hand, the active stress can have strong sign-preserving properties, possibly stronger than the ones typically advocated for the standard stress, as the due weakness will be ensured by the standard part of the stress. Provided that

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<sup>2</sup>A neo-Hookean hyperelastic material is incompressible and the Lagrange multiplier corresponding to such a constrain should appear in the Cauchy stress (5.2). However, we are here interested in investigating the rank-one ellipticity of the stress tensor, the pressure does not perform any work because  $-p\mathbf{F}^{-T} : \mathbf{H} = 0$  and we omit such a term for the sake of simplicity. The same argument applies for possible incompressible materials of the previous sections.

the sought mathematical characterization is abided, the active stress approach ensures the flexibility to reproduce the observed physiological behavior.

The active strain approach is mathematically more robust, as frame invariance and rank–one ellipticity are simply inherited from the corresponding properties of the standard strain energy of the material. Conversely, the analysis of the physiological predictions in terms of dependence of the active force on the stretch is more involved. The active strain approach is more rigid and allows no chance for modelling the physiological behavior after that the inert properties of the material are prescribed. When a reinterpretation of the active strain in terms of active stress is possible, no new free parameters are to be fitted: the new dynamic contribution naturally arises from the visible stretch, because the kinematics of the microstructure is directly encoded in the equations. While the mathematical derivation of the model is more elegant, as no active stress function is to be tuned, the physiological effectiveness of the obtained model remains to be addressed. A few investigations into the physiological relevance of the multiplicative decomposition has been done for smooth muscles with promising results, see, e.g., [13] and [23].

**Acknowledgements** We are indebted with Fabio Nobile, Paolo Biscari, Maurizio Vianello, Ricardo Ruiz Baier and Simone Rossi for fruitful discussions about the content of this paper. This work has been supported by the ERC Advanced Grant *Mathcard* (number 227058).

## Appendix A

Introduce  $\mathbf{e}_1 = (1, 0, 0)^T$  and let  $\mathbf{Q}$  be the rotation such that  $\mathbf{Q}\mathbf{e}_1 = \mathbf{n}$ . The following identity holds:

$$\begin{aligned} (\mathbf{1} - \gamma \mathbf{n} \otimes \mathbf{n})^{-1} &= (\mathbf{1} - \gamma \mathbf{Q}\mathbf{e}_1 \otimes \mathbf{Q}\mathbf{e}_1)^{-1} = (\mathbf{Q}\mathbf{Q}^T - \gamma \mathbf{Q}(\mathbf{e}_1 \otimes \mathbf{e}_1)\mathbf{Q}^T)^{-1} \\ &= (\mathbf{Q}(\mathbf{1} - \gamma \mathbf{e}_1 \otimes \mathbf{e}_1)\mathbf{Q}^T)^{-1} = \mathbf{Q}(\mathbf{1} - \gamma \mathbf{e}_1 \otimes \mathbf{e}_1)^{-1}\mathbf{Q}^T \\ &= \mathbf{Q}\left(\mathbf{1} + \frac{\gamma}{1-\gamma}\mathbf{e}_1 \otimes \mathbf{e}_1\right)\mathbf{Q}^T = \mathbf{1} + \frac{\gamma}{1-\gamma}\mathbf{n} \otimes \mathbf{n}. \end{aligned}$$

## Appendix B

The Cauchy stress is

$$\mathbf{T} = \det(\mathbf{F}_a) \frac{\partial \mathcal{W}}{\partial \mathbf{F}_e} \mathbf{F}_a^{-T} \mathbf{F}^T = \det(\mathbf{F}_a) (\mu_1 \mathbf{F}_e + \mu_2 \mathbf{F}_e \mathbf{n} \otimes \mathbf{n}) \mathbf{F}_a^{-T} \mathbf{F}^T.$$

The first term at the right hand side is

$$\begin{aligned} \det(\mathbf{F}_a) \mathbf{F}_e \mathbf{F}_a^{-T} \mathbf{F}^T &= \det(\mathbf{F}_a) \mathbf{F} \mathbf{F}_a^{-1} \mathbf{F}_a^{-T} \mathbf{F}^T \\ &= (1-\gamma) \mathbf{F} \left( \mathbf{1} + \frac{\gamma}{1-\gamma} \mathbf{n} \otimes \mathbf{n} \right) \left( \mathbf{1} + \frac{\gamma}{1-\gamma} \mathbf{n} \otimes \mathbf{n} \right)^T \mathbf{F}^T \\ &= (1-\gamma) \mathbf{F} \mathbf{F}^T + \gamma \frac{2-\gamma}{1-\gamma} \mathbf{F} \mathbf{n} \otimes \mathbf{F} \mathbf{n}. \end{aligned}$$

Noting that

$$\mathbf{F}_e \mathbf{n} = \mathbf{F} \mathbf{F}_a^{-1} \mathbf{n} = \frac{1}{1-\gamma} \mathbf{F} \mathbf{n},$$

the second term at the right hand side rewrites

$$(1-\gamma) \mathbf{F}_e \mathbf{n} \otimes \mathbf{n} \mathbf{F}_a^{-T} \mathbf{F}^T = (1-\gamma) \mathbf{F}_e \mathbf{n} \otimes \mathbf{F}_e \mathbf{n} = \frac{1}{1-\gamma} \mathbf{F} \mathbf{n} \otimes \mathbf{F} \mathbf{n}.$$

## References

- [1] Ambrosi, D., Arioli, G., Nobile, F., and Quarteroni, A.: Electromechanical coupling in cardiac dynamics: the active strain approach, *SIAM J. Appl. Math.*, **71**, 605–621 (2011)
- [2] Antman, S. S.: *Nonlinear Problems of Elasticity*. Springer, New York (2005)
- [3] Böl, M., Abilez, O. J., Assar, A. N., Zarins, C. K., and Kuhl, E.: In vitro/in silico characterization of active and passive stresses in cardiac muscle. *Int. J. Multiscale Comput. Eng.* (2011), in press
- [4] Campbell, K. B., Simpson, A. M., Campbell, S. G., Granzier, H. L., and Slinker, B. K.: Dynamic left ventricular elastance: a model for integrating cardiac muscle contraction into ventricular pressure–volume relationships. *J. Appl. Phys.*, **104**, 958–975 (2008)
- [5] Cherubini, C., Filippi, S., Nardinocchi, P., and Teresi, L.: An electromechanical model of cardiac tissue: Constitutive issues and electrophysiological effects. *Prog. Biophys. Mol. Biol.*, **97**, 562–573 (2008)
- [6] DiCarlo, A. and Quiligotti, S.: Growth and balance. *Mech. Res. Commun.*, **29**, 449–456 (2002)
- [7] Downey, J. M.: The Mechanical Activity of the Heart. In: Johnson, L. R. (ed.) *Essential Medical Physiology*, 3rd ed., pp. 201–213. Elsevier (2003)
- [8] Göktepe, S. and Kuhl, E.: Electromechanics of the heart: a unified approach to the strongly coupled excitation–contraction problem. *Comput. Mech.*, **45**, 227–243 (2010)
- [9] Holzapfel, G. A. and Ogden, R. W.: Constitutive modelling of passive myocardium: a structurally based framework for material characterization. *Philos. Trans. R. Soc. London, Ser. A*, **367**, 3445–3475 (2009)
- [10] Iribe, G., Helmes, M., and Kohl, P.: Force–length relations in isolated intact cardiomyocytes subjected to dynamic changes in mechanical load. *Am. J. Physiol. Heart Circ. Physiol.*, **292**, H1487–H1497 (2007)
- [11] I-Shih Liu: *Continuum Mechanics*. Springer, New York (2002)
- [12] Merodio, J. and Ogden, R. W.: Mechanical response of fiber–reinforced incompressible nonlinearly elastic solids. *Int. J. Non Linear Mech.*, **40**, 213–227 (2005)
- [13] Murtada, S., Kroon, M., and Holzapfel, G. A.: A calcium–driven mechanochemical model for prediction of force generation in smooth muscle. *Biomech. Model. Mechanobiol.*, **9**, 749–762 (2010)
- [14] Nardinocchi, P. and Teresi, L.: On the Active Response of Soft Living Tissues, *J. Elast.*, **88**, 27–39 (2007)
- [15] Nardinocchi, P., Teresi, L., and Varano, V.: Myocardial Contractions and the Ventricular Pressure–Volume Relationship. *arXiv:1005.5292v1 [q-bio.TO]* (2010)
- [16] Niederer, S. A. and Smith, N. P.: An improved numerical method for strong coupling of excitation and contraction models in the heart. *Prog. Biophys. Mol. Biol.*, **96**, 90–111 (2008)
- [17] Nobile, F., Quarteroni, A., and Ruiz-Baier, R.: Numerical simulation of an active strain electromechanical model for cardiac tissue, submitted (2011)

- [18] Panfilov, A. V., Keldermann, R. H., and Nash, M. P.: Self-Organized Pacemakers in a Coupled Reaction-Diffusion-Mechanics System. *Phys. Rev. Lett.*, **95**, 258104 (2005)
- [19] Pathmanathan, P., Chapman, S. J., Gavaghan, D. J., and Whiteley, J. P.: Cardiac Electromechanics: The Effect of Contraction Model on the Mathematical Problem and Accuracy of the Numerical Scheme. *Q. J. Mechanics Appl. Math.*, **63**, 375–399 (2010)
- [20] Redaelli, A. and Pietrabissa, R.: A Structural Model of the Left Ventricle Including Muscle Fibres and Coronary Vessels: Mechanical Behaviour in Normal Conditions, *Meccanica*, **32**, 53–70 (1997)
- [21] Rodriguez, E. K., Hoger, A., and McCulloch, A. D.: Stress-dependent finite growth in soft elastic tissues. *J. Biomech.*, **27**, 455–467 (1994)
- [22] Smith, N. P., Nickerson, D. P., Crampin, E. J., and Hunter, P. J.: Multiscale computational modelling of the heart. *Acta Numer.*, **13**, 371–431 (2004)
- [23] Stålhand J., Klarbring A., and Holzapfel G. A.: Smooth muscle contraction: Mechanochemical formulation for homogeneous finite strains. *Prog. Biophys. Mol. Biol.*, **96**, 465–481 (2008)
- [24] Taber, L. A.: Towards a unified theory for morphomechanics. *Philos. Trans. R. Soc. London, Ser. A*, **367**, 3555–3583 (2009)
- [25] Taber, L. A., Perucchio, R.: Modeling Heart Development. *J. Elast*, **61**, 165–197 (2000)
- [26] Whiteley, J., Bishop, M., and Gavaghan, D.: Soft Tissue Modelling of Cardiac Fibres for Use in Coupled Mechano-Electric Simulations. *Bull. Math. Sci.*, **69**, 2199–2225 (2007)



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