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A structural constitutive model for smooth muscle contraction in biological tissues

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ABSTRACT

A structural constitutive model that characterizes the active and passive responses of biological tissues with smooth muscle cells (SMCs) is proposed. The model is formulated under the assumption that the contractile units in SMCs and the connected collagen fibers are the active tissue component, while the collagen fibers not connected to the SMCs are the passive tissue component. An evolution law describing the deformation of the active tissue component over time is developed based on the sliding filament theory. In this evolution law the contraction force is the sum of a motor force that initiates contraction, a viscous force that describes the actin–myosin filament sliding, and an elastic force that accounts for the deformation of the cross-bridges. The mechanical response of the collagen fibers is governed by the fiber recruitment process: collagen fibers support load and behave as a linear elastic material only after becoming taut. The proposed structural constitutive model is tested with published active and passive, uniaxial and biaxial experimental data on pig arteries.

1. Introduction

Biological hollow structures such as blood vessels, airways, gastrointestinal tracts and pelvic organs are mainly composed of an extracellular matrix and smooth muscle cells (SMCs). The extracellular matrix contains mainly elastin and collagen fibers embedded in the so-called *ground substance* and controls the passive deformation of these structures. The SMCs govern and maintain the active deformation. They have contractile units that function as sarcomeres in skeletal muscles and are composed of actin filaments, myosin filaments, and dense bodies [1,2] (Fig. 1(a)). The actin filaments are anchored to dense bodies. The dense bodies serve to connect the contractile units throughout the cell and are attached to the cell membrane [3]. Each myosin filament is aligned between two actin filaments, with the myosin heads uniformly spaced between these filaments [3]. When the intracellular calcium concentration increases due to electric, chemical, and mechanical stimuli, cross-bridges form between the myosin heads and the actin filaments, leading to SMC contraction [4]. SMCs generate a contraction force that is comparable to the force generated by skeletal muscle cells. However, unlike skeletal muscle cells, SMCs maintain this contraction force over a longer time, and they have a much lower contraction speed so as to accomplish their physiological functions (e.g., maintain proper pressure in blood vessels, propelling food in the gastrointestinal tracts) [5].

The contraction mechanism in skeletal muscle has been explained by H.E. Huxley, A.F. Huxley and co-authors [6–9], who proposed the so-called *sliding-filament theory*. According to this theory, the contraction force in skeletal muscle is generated by the attachment of myosin heads to actin filaments (i.e., the formation of cross-bridges) during actin–myosin filament sliding. Based on the sliding-filament theory, Hai and Murphy presented a new model that include the *latch state* introduced by Dillon et al. [10,11] to capture the characteristic cross-bridge kinetics of the SMCs [12]. In this state, a high contraction force is maintained at a very low or even zero contraction speed.

Constitutive models that describe the active mechanical contribution of SMCs in biological hollow structures have been proposed over the years. The passive response has been usually assumed to be due to the collagen and elastin fibers, while the active response has been assumed to be determined by the contractile units in SMCs. For vascular tissue, Rachev and Hayashi [13] introduced an *ad hoc* parameter that defined the contractile activity of SMCs to model the active stress, and adopted a parabolic function for the typical isometric length–tension data. Later, Zulliger et al. [14] proposed a structural model for arteries that included the mechanical contribution of SMCs. The active stress was defined by introducing two functions that described the muscle tone level and the isometric length–tension data. To more precisely account for the contraction mechanisms of SMCs, a mechano-chemical model considering Ca^{2+} concentration and temperature was proposed by Stålhand et al. [15]. In this model, the SMC deformation was assumed to be the result of cross-bridge deformation and filament sliding. Recently, Murtada et al. [16,17]

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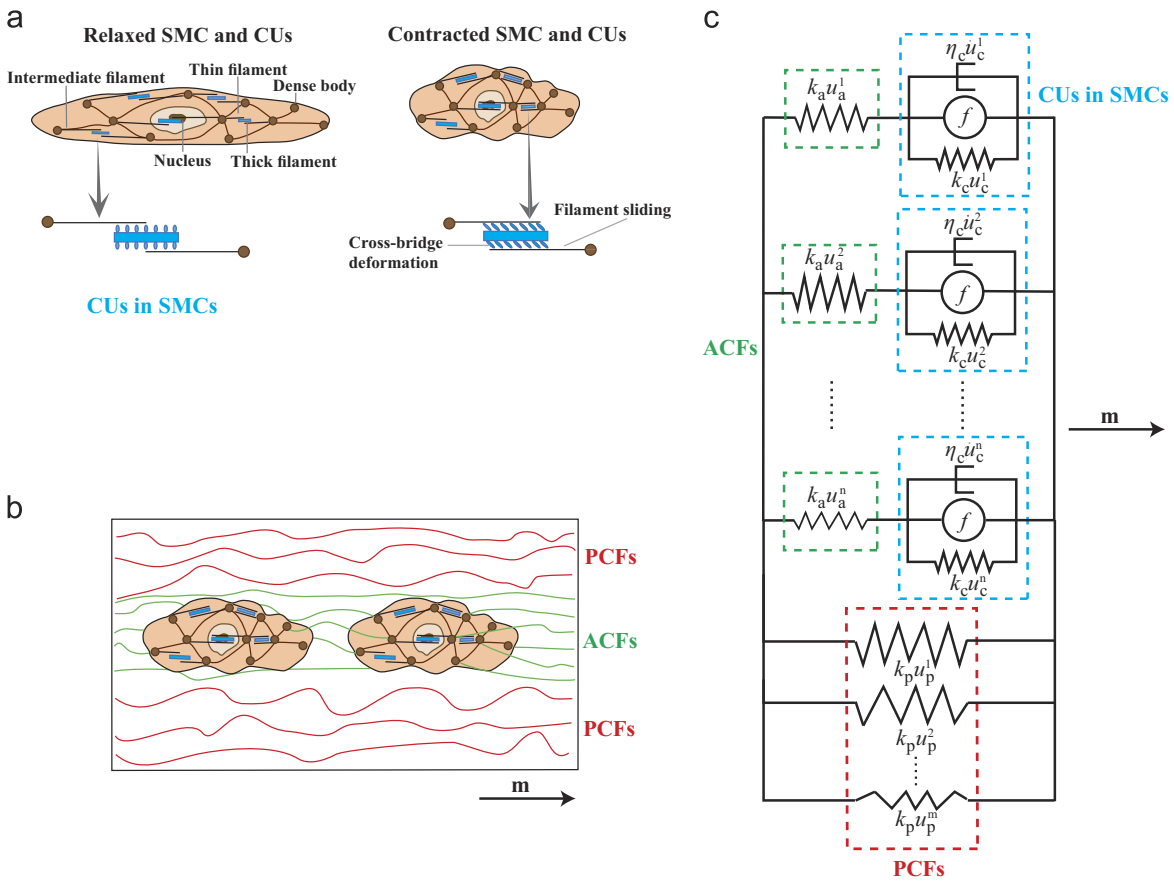

Fig. 1. (a) Smooth muscle cells (SMCs) and contractile units (CUs). (b) Active collagen fibers (ACFs), passive collagen fibers (PCFs), and SMCs. (c) Model schematic for PCFs, ACFs, and CUs in SMCs showing only a discrete number of elements: n elements for the ACFs (or CUs) and m elements for the PCFs. In the proposed model, the continuous recruitment of these elements under load is described by a probability density function. *Note:* All the elements are oriented along the unit vector **m** in the reference configuration.

proposed a new theoretical framework in which the active response was defined by considering the dispersion of contractile units, actin–myosin filament overlap and sliding, and chemical activity as done by Hai and Murphy [12]. More specifically, they introduced a phenomenological parabolic filament overlap function [17], which captured the length–tension data in isometric experiments. Finally, Chen et al. [18] developed a constitutive model that also incorporated the experimentally measured orientation of vascular SMCs.

In this study, a new structural constitutive model for the active and passive mechanical behavior of biological tissues containing SMCs is proposed. The SMC contraction force is assumed to be equal to the force acting on the surrounding collagen fibers. This assumption is justified by the fact that the contraction force generated by SMCs can be transmitted, via their connection to the dense bodies, to the extracellular matrix [1]. Thus, the active stress can be computed from the stress of the collagen fibers that are connected to the SMCs, without introducing a chemical kinetics model as done by other investigators [16,17]. Within the framework of Hill's three-element model [19], we develop an evolution law for the deformation of SMCs and connected collagen fibers. Following the sliding filament theory, in this evolution law the contraction force is the sum of a motor force that initiates contraction, a viscous force that describes the actin–myosin filament sliding, and an elastic force that accounts for the cross-bridge deformation. The passive response of the collagen fibers is captured by the non-linear elastic model proposed by De Vita [20]. The proposed structural constitutive model is then tested using uniaxial isometric length–tension [17] and isotonic quick-release experimental data [10] on pig carotid arteries and biaxial isometric inflation–extension experimental data on pig coronary arteries [18].

2. Model formulation

In the proposed model, the mechanical behavior of biological tissues with SMCs is assumed to be determined by the collagen fibers. We assume that there are two different types of collagen fibers based on their interaction with SMCs (Fig. 1(b)). Collagen fibers of the first type are directly connected to SMCs. These collagen fibers determine the active mechanical response of the tissues. The activation of SMCs is assumed to be transmitted to the neighboring collagen fibers. For this reason, the collagen fibers connected to SMCs are called the *active collagen fibers* (ACFs). Collagen fibers of the second type are not connected to SMCs. These determine the passive mechanical response of the tissues and are called the *passive collagen fibers* (PCFs). The mechanical contributions of other components (e.g., ground substance or elastin) are neglected. In summary, the active and passive mechanical behaviors of biological tissues with SMCs are determined by the ACFs and PCFs, respectively.

2.1. Constitutive model for the ACFs and PCFs

Within the framework of non-linear elasticity, the active or passive first and second Piola–Kirchhoff stress tensors, **P** and **S**, respectively, are expressed as [21]

$$\mathbf{P} = -p\mathbf{F}^{-\mathrm{T}} + 2\mathbf{F}\cdot\frac{\partial W}{\partial \mathbf{C}}, \quad \mathbf{S} = -p\mathbf{C}^{-1} + 2\frac{\partial W}{\partial \mathbf{C}}, \tag{1}$$

where p is the Lagrange multiplier that accounts for incompressibility, **F** is the deformation gradient, $\mathbf{C} = \mathbf{F}^{\mathrm{T}}\cdot\mathbf{F}$ is the right Cauchy–Green strain tensor, and W is the strain energy of ACFs