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Mechanical response of human female breast skin under uniaxial stretching

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ABSTRACT

Skin is a complex material covering the entire surface of the human body. Studying the mechanical properties of skin to calibrate a constitutive model is of great importance to many applications such as plastic or cosmetic surgery and treatment of skin-based diseases like decubitus ulcers. The main objective of the present study was to identify and calibrate an appropriate material constitutive model for skin and establish certain universal properties that are independent of patient-specific variability. We performed uniaxial tests performed on breast skin specimens freshly harvested during mastectomy. Two different constitutive models – one phenomenological and another microstructurally inspired – were used to interpret the mechanical responses observed in the experiments. Remarkably, we found that the model parameters that characterize dependence on previous maximum stretch (or preconditioning) exhibited specimen-independent universal behavior.

1. Introduction

The skin is the largest organ of the human body. Its main function is to protect the body against external influences. Depending on its purpose and location on the body, the mechanical behavior and thickness of skin vary. For example, the eyelids, whose main function is to blink (folding and unfolding), have a thickness of only 0.5 mm, while the skin on the soles of the feet, which must be able to resist cuts and abrasions, is at least 4 mm thick. Understanding the mechanical behavior of skin is important to many applications, such as cosmetic and reconstructive surgery, healing issues following surgical operations, and the treatment of skin-based diseases. The *in vivo* mechanical behavior of skin is described as heterogeneous, anisotropic, non-linear, and viscoelastic (Lanir and Fung, 1974; Dunn et al., 1985; Silver et al., 2001; Annaidh et al., 2012). Many factors such as age, biological sex, and hydration also affect the skin's response.

Tensile tests – uniaxial and biaxial – are important methods for characterizing soft tissues such as skin. Such mechanical tests help to develop an understanding of the normal functional response of this organ and predict its response in cases of medical interventions such as surgery. Many experiments have been performed on skin to understand its complex mechanical behavior (see for example, porcine: Shergold et al., 2006 and Khatam et al., 2014; murine: Munoz et al., 2008; human: Abas and Barbenel, 1982; Dunn and Silver, 1983; Escoffier et al., 1989; Edwards and Marks, 1995; Clark et al., 1996; Reihsner and Menzel, 1996; Bischoff et al., 2000; Silver et al., 2001; Hendriks et al., 2003; Kvistedal and Nielsen, 2009; Annaidh et al., 2012; Groves et al., 2013 and Tonge et al., 2013a,b; and rabbit: Lanir and Fung, 1974). Although it is generally accepted that uniaxial tension tests are insufficient to characterize skin completely, such tests are still typically performed on skin specimens *in vitro* (see for example, Moronkeji and Akhtar, 2015). There are numerous *in vivo* tests on skin as well since this will provide important characterization under physiologically correct conditions (see for example, Abas and Barbenel, 1982; Manschot and Brakkee, 1986; Escoffier et al., 1989; Kvistedal et al., 2009).

The microstructure and biomechanical properties of skin (and other soft biological tissues) have been studied by numerous investigators, and there exists a common understanding of both (see for example, Gibson et al., 1965; Fung, 1967; Harkness, 1971; Wilkes et al., 1973; Sanders and Goldstein, 1995; Annaidh et al., 2012; Menon et al., 2012; Tonge et al., 2013a,b; Caro-Bretelle et al., 2015, 2016; Bancelin et al., 2015). A succinct summary of skin composition is provided by Sanders and Goldstein (1995): skin is composed of collagen (27% to 39% by volume, 75% to 80% of fat-free dry weight), elastin (0.2% to 0.6% by volume, 4% of fat-free dry weight), glycosaminoglycans (0.03% to

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0.35% by volume), and water (60% to 72% by volume). Different constituents govern the typical mechanical response of skin at different load levels. In addition, skin contains cells such as fibroblasts (for generating capillary and thermoregulatory blood vessels and elastin, collagen, and glycosaminoglycans as needed for growth, adaptation, and remodeling), and macrophages, and leukocytes; however, these are considered not to influence the mechanical response directly (see discussion in Pegg, 2006).

The structure of the constituents of skin is important for determining its response to mechanical stress. Elastin fibers form a network and provide the ability to recoil; this network is embedded in the network of crimped collagen fibers that are themselves cross-linked. While early research suggested that the collagen fibers are initially randomly oriented (see Fig. 5 of Dunn et al., 1985), more recent work has provided measurements that indicate a systematic orientation distribution (Annaidh et al., 2012; Bancelin et al. 2015). Nevertheless, a sharp increase in stiffness with deformation is generated as the average stretch increases beyond some threshold, primarily due to uncrimping and reorientation of the collagen fibers with deformation. The remaining constituents, water and the glycosaminoglycans, provide viscous properties to skin. This composite structure of skin results in nonlinear, time-dependent mechanical behavior that can include elastic response, viscoelasticity, and damage (Dunn et al. 1985; Sanders and Goldstein, 1995; Bischoff et al., 2000; Silver et al., 2001; Munoz et al., 2008).

According to Fung (1967), the *intrinsic elastic response* of a biomaterial (such as skin), devoid of any time-dependent or inelastic response, can be extracted from a preconditioned specimen. This intrinsic elastic response plays a crucial role in the overall physiological response. A schematic diagram of the typical uniaxial response of skin is shown in Fig. 1, indicating the variation of the nominal stress with the stretch: Four different phases are commonly identified in stress-stretch diagrams of preconditioned response. Phase 1 corresponds to the stretching of the elastin network, the most compliant of the skin constituents. Typical modulus in Phase 1 is in the range of 15–20 kPa and this low modulus persists until a stretch level of about 1.3. Note that this network modulus is significantly smaller than the elastic modulus of elastin itself, which is around 0.6 MPa (Fung, 1993) and retains a nearly linear elastic behavior for a stretch of about 1.6. Beyond this phase, the collagen fibers begin reorienting and uncrimping themselves in the direction of the stretching, exhibiting their higher resistance to stretching and contributing to a nonlinear, stiffening response; hence, Phase 2 represents a transition region where more and more collagen fibers become aligned with increasing stretch. We will examine this through a fiber recruitment model in Section 2.3. Phase 3 represents the stiffest response observed, corresponding to nearly fully oriented collagen; the response is nearly linear with a modulus of about few hundred MPa, about three to four orders of magnitude greater than in Phase 1. Finally, damage to the network occurs beyond a maximum stress level corresponding to the strength of the skin, and a softening response is observed in Phase 4. It is commonly considered that the physiological state of the skin lies somewhere between Phases 2 and 3 (Abas and Barbenel, 1982). It should be noted that the roles of elastin and collagen are similar in the preconditioned and first (native) loading responses; the only differences are slightly larger moduli in each segment and a smaller stretch level at which these transitions occur in the first loading response. The unloading and reloading response stabilizes along the line '1–2–3' and corresponds to the preconditioned response up to the maximum stretch imposed.

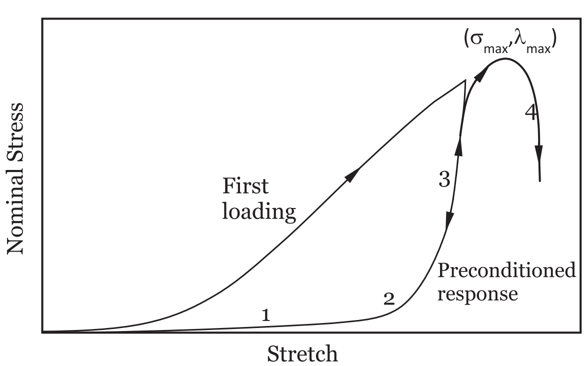

Fig. 1. Typical variation of the nominal stress with stretch for skin specimens for the first loading, the preconditioned response and loading up to failure. Phases 1 through 4 are identified in the preconditioned response. The maximum stress σ_{max} occurs at a stretch λ_{max} that corresponds to the maximum possible stretch without generating permanent damage.

The significant difference in the stress level at a given stretch between the first loading response and the preconditioned response (sometimes called strain-softening) is attributed to viscoelasticity (Lanir and Fung, 1974) or to damage that is analogous to Mullins's effect in rubber (Emery et al., 1997; Munoz et al., 2008; Johnson and Beatty, 1993; Caro-Bretelle et al., 2015, 2016). Lanir and Fung (1974) observed full recovery of strain-softening in rabbit skin after several hours, if all the strains experienced were always positive (note that this is violated in simple uniaxial tension where the transverse strain is negative). If loading is continued monotonically, a peak stress level is attained beyond which the skin becomes damaged and fails (Phase 4). While preconditioned specimens provide a repeatable characterization of subsequent response, it is not apparent that this is the response that is important *in vivo* in all applications, especially if there is long-term recovery of both dimensions (as indicated in Lanir and Fung, 1974) and response. In addition, in a recent article, Tonge et al. (2013a,b) investigated the behavior of human skin under biaxial loading in a bulge test where the specimen experiences non-uniform strain distribution; their results indicate that the effects of preconditioning on the structural response are negligible.

The use of constitutive models, posed in the framework of the theory of finite elasticity through a strain-energy density function, brings consistency to the measured data and provides a way to generalize the specific results obtained in the uniaxial tensile tests. There are numerous strain energy density functions that have been proposed to model material behavior for soft materials, for example, the neo-Hookean, Mooney-Rivlin, Ogden, Valanis-Landel (see Ogden, 1997 for a discussion of these models), Lopez-Pamies (2010), and other models describe the strain energy density functions applicable to typical elastomers. For soft tissues, Fung (1967) introduced a model that captures the exponential dependence of the stress on the deformation; many others have followed this model and there exists a vast array of such strain-energy density functions in the literature. Some of these models are derived from micromechanical considerations of the anisotropic structure of the materials, while others are purely phenomenological. Here, we consider two models, one by Hart-Smith (1966) and another by Rausch and Humphrey (2016) for interpreting experimental measurements; these models are described fully in Section 2.3.

Using these models, we investigated the mechanical response of human female breast skin obtained during mastectomy. While the anisotropic material behavior of skin necessitates the use of biaxial testing to capture its constitutive behavior fully, the lack of availability of large areas of skin for such testing limits biaxial testing to a few samples. Therefore, we embarked on uniaxial tests first to understand and characterize the mechanical response under tensile loading so that future biaxial tests could be performed more efficiently on the few available specimens. The main objective of the present study was to identify and calibrate an appropriate material constitutive model for skin and establish certain universal properties that are independent of patient-specific variability. While there are numerous phenomenological and mechanistic models of the mechanical behavior of soft tissues in general, and skin in particular, we will demonstrate that a universal model of response can be obtained with material properties dependent only on the previous maximum stretch level attained.