A modeler's guide to soft tissue mechanics

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Abstract

Soft tissue mechanical behavior and its change with age, physiological adaption, and disease, are key to our health and survival. Soft tissues are divided in four main categories, epithelial, muscle, connective, and nervous system tissues. Different types of tissues have unique composition and microstruture to perform their specific functions. Musculoskeletal and connective soft tissues, in particular, have evolved to address important mechano-physiological needs. All soft tissues, whether or not their primary function is mechanical in nature, show extreme mechanics, with large deformation, nonlinear stress-strain stiffening, various modes of energy dissipation such as viscoelasticity and damage, and, most remarkably, show the ability to adapt to external stimulus through growth and remodeling. This chapter outlines the essential theoretical frameworks for modeling the complex behavior of soft tissue. The role of data-driven tools as well as the soft tissues that have received increasing attention in recent years are also discussed.

Keywords: Tissue biomechanics, hyperelasticity, hyper-viscoelasticity, fractional viscoelasticity, continuum damage mechanics, growth and remodeling, reactive mixtures, mechanobiology, multiscale modeling, data-driven material modeling

1. Introduction

Soft tissue mechanical response and its change with aging, physiological adaptation, and disease, are key to our health, well-being, and survival. There are four main types of soft tissue: epithelial, muscle, connective, and nervous system tissues [1]. Each of these types has their unique function, which is also reflected in composition, structure, and mechanical response.

Epithelial tissues are highly cellular. They line various organs and constitute the bulk of glandular organs [2, 3]. Epithelia serve transport regulation roles [4]. For example the epithelial linings of arteries and intestines are tasked with exchange of nutrients and chemical signals between two interfaces [5]. Epithelial tissue in organs such as pancreas or liver secrete important hormones such as insulin and insulin-like growth factor 1 respectively. Despite a predominant transport role, epithelial tissue show complex mechanical response that allows them to operate effectively at large deformations [2]. Cell packing in epithelial tissue and overall epithelial tissue geometry are also remarkably intricate and entail complex morphogenetic programs in which mechanics plays a central role [6]. Muscle tissues give the active force needed for locomotion. Muscles, together with tendons, ligaments and cartilage are the soft tissues directly involved with locomotion [7]. Muscles have a unique active unit called the sarcomere, which shortens upon electrical activation, developing large amounts of tension along the muscle fibers [8, 9]. Muscle attaches to bone through tendons, a type of connective tissue; and ligaments, another connective tissue, connect two bones directly [10]. Cartilage tissue is located at the end of bones, and is important for bone-to-bone motion by enabling a low friction interface at joints [11]. Cartilage complex microstructure also allows for shock absorption [12]. Connective tissues are the most varied because they have a supportive role to all different kinds of tissues. For example, another connective tissue is the dermis in the skin. Other examples include the connective tissue in the intermediate layers of the arteries, heart valves, the amnion during pregnancy, among other examples [13, 14, 15]. Connective tissues are collagen based, giving them the ability to support structural function. The tissues of the central nervous system do not have a mechanical support role. Nonetheless, their mechanical response is important in the context of injury, e.g. traumatic brain injury [16, 17]. Morphogenesis and degeneration of central nervous system tissues also entails extreme mechanics [18]. In summary, soft tissues have a wide range of structure and function. In some cases the function is indeed biomechanical in nature, while in other cases, even if the tissue does not serve a primary mechanical role, it still has to show extreme mechanical response and mechanobiological adaptation.

Soft tissues undergo large deformation and show nonlinear stress-strain response. Thus, linear elasticity is ruled out as a suitable framework to describe soft tissue mechanics [19]. A common starting point to model soft tissue is hyperelasticity. While there are some connections in the literature

to linear elasticity theory, e.g. references to Poisson ratio and Young's modulus, these properties do not truly describe the finite deformation regime and nonlinearity of soft tissue and should be treated as rough albeit useful approximations [20]. In addition to hyperelastic behavior -which assumes a strain energy potential such that unloaded tissues return fully to their original state upon unloading-, inelastic behavior of soft tissue is also essential [21]. Examples of inelastic response includes damage degradation, viscoelasticity, and fracture. All these problems have to be modeled in the context of finite deformations [22].

Tissues are hydrated materials. In some cases it is possible to ignore the fluid phase of tissues and focus on their mechanics as a homogenized solid. However, for some tissues and in particular contexts, the relative fluid transport in the tissue with respect to the solid matrix is key for understanding the response under compression, dynamic loading, volume changes, and drug transport [23]. For instance in cartilage, multi-phasic theories are needed to explain the performance of this tissue in compression at our joins [24, 25]. Bi-phasic theories are also needed for subcutaneous tissue in the context of drug delivery [26, 27].

Soft tissues often show anisotropy. Ultimately, the macroscopic mechanical response of tissues is a reflection of their microstructure. For connective and musculoskeletal tissues such as ligaments and tendons, the most prominent microstructure feature is the alignment of collagen fibers which constitute the majority of the dry weight of these tissues [28]. Preferred collagen orientations are usually linked to the tissue's mechanical function [29, 30]. For instance, in tendons and ligaments, the loading direction along a particular direction coincide with the collagen fiber reinforcements in that direction. Nevertheless, some ligaments can exhibit complex fiber alignment if they are subject to complex loading modes, e.g. the ligaments in the knee joint twist around rather than connecting the femur and tibia in a straight line [31]. Epithelial tissues tend to show isotropic or transversely isotropic response because cell packings tend to be isotropic in a bulk tissue such as adipose tissue, or they form a thin membrane with mostly isotropic properties on the plane of the membrane [3, 2]. Brain is also mostly treated as isotropic, although there is some role of axons in the mechanical response which can introduce mild anisotropy [32]. In muscles, sarcomeres also arrange into fibers with well-defined orientations, leading to anisotropic or transversely isotropic behavior [8].

What truly distinguishes tissues from many structural materials is their

ability to adapt to mechanical cues over time. This phenomenon is termed growth and remodeling [33]. Tissues are alive. At the microscopic scale, cells, the units of life, on the order of tens of microns, sense and respond to their immediate microenvironment by deposition new material, degrading existing material, and exerting forces that permanently change the microstructure geometry over time [34, 35, 36].

Organ systems, even small ones, contain multiple tissues tightly packed together. For example skin protects us mechanically from the environment, regulates transport exchange with the outside world, and also has a role in thermal regulation and the sense of touch [37, 38, 39, 40]. To do so it requires multiple substructures. Skin has a top epithelial layer of keratinocyte cells, a connective tissue layer below, the dermis, which is the load bearing layer, and a subcutaneous layer made of an adipocyte cell packing below, with a primary role in thermal regulation and energy storage. Appendages in skin such as glands, touch receptors, and hair follicles, endow this tissue with its wide ranging set of functions [41]. Even trying to focus on the dermis alone, regional changes in collagen ultrastructure as well as other factors of structural composition of the tissue lead to different mechanical behavior from one location to another [42]. Thus, a common strategy to model soft tissue is through multiscale approaches [43].

The chapter is divided as follows. From a theory of mechanics standpoint we build up in complexity, starting from hyperelastic modeling, we move on to viscous response, then to damage. We then switch to multi-phasic theories. The problem of active elements, primarily for muscle tissue, is introduced next. This is followed by reviewing modeling frameworks for the unique capacity of tissue for growth, remodeling and wound healing. This is not the end of the chapter, as we reserve a last section to highlight new modeling frameworks that reflect recent trends in data-driven modeling and machine learning for computational mechanics. Throughout the chapter, we state both the general equations of a given theory, and then emphasize specific models used in the context of soft tissue biomechanics.

2. Hyperelastic behavior

Hyperelasticity is formally defined in terms of an energy potential that allows us to relate the stress at a point in the material to the deformation at that point. If we denote the first Piola Kirchhoff stress with $\mathbf{P}$ and the deformation gradient with $\mathbf{F}$, then hyperelasticity posits the existence of a

scalar-valued potential function known as the *strain energy density function* (SEDF) [44], denoted as $\Psi(\mathbf{F})$, such that

$$\mathbf{P} = \frac{\partial \Psi(\mathbf{F})}{\partial \mathbf{F}} \,. \tag{1}$$

The most important implication of this equation is that in hyperelasticity, the relationship between deformation and stress is *unchanging*. This is as opposed to other constitutive models such as viscoelasticity and continuum damage modeling, where Ψ evolves with time, loading history or the state of damage in the material (as we will see later on).

The deformation gradient $\mathbf{F}$ contains information both about stretching and rotations of a point in the material, however, Ψ has to remain invariant of rigid body rotations. To this end, the SEDF is often expressed as a function of the *right Cauchy-Green deformation tensor*, $\mathbf{C} = \mathbf{F}^\top \mathbf{F}$. Using this form of the SEDF, the *Second Piola Kirchhoff Stress*, $\mathbf{S}$, can be obtained as

$$\Psi = \Psi(\mathbf{C}), \quad \mathbf{S} = \frac{1}{2} \frac{\partial \Psi(\mathbf{C})}{\partial \mathbf{C}} \,. \tag{2}$$

2.1. Incompressible hyperelasticity

Eq. (2) provides the most general form of the relationship between $\mathbf{C}$ and $\mathbf{S}$ in hyperelasticity when $\mathbf{C}$ is arbitrary. However, under the condition of incompressibility, the elements of $\mathbf{C}$ are not arbitrary. In this case the relationship between $\mathbf{C}$ and $\mathbf{S}$ has the following form [45]

$$\mathbf{S} = 2 \frac{\partial \hat{\Psi}(\mathbf{C})}{\partial \mathbf{C}} + pJ\mathbf{C}^{-1} \tag{3}$$

where p is a pressure Lagrange multiplier which can be understood as a hydrostatic stress to resist compression, $J = \det \mathbf{F}$ is the volume change and $\hat{\Psi}$ is a *distortional* energy function that depends on $\mathbf{C}$ only through the isochoric part of $\mathbf{C}$, i.e.,

$$\begin{aligned} \hat{\Psi}(\mathbf{C}) &= \Psi(\hat{\mathbf{C}}) \\ \hat{\mathbf{C}} &= (\det \mathbf{C})^{-1/3} \mathbf{C} \,. \end{aligned}$$

Using the relationship in Eq. (3) requires determining the pressure p. In some special cases, such as biaxial deformation of a thin membrane under plane-stress conditions, p can be determined from boundary conditions.

However, this is not possible in general. Therefore, a *nearly incompressible* approach is followed in most practical applications [46]. In nearly incompressible hyperelasticity of soft tissue, the SEDF is constructed by adding a volumetric term to the distortional energy, i.e.,

$$\Psi(\mathbf{C}) = \hat{\Psi}(\mathbf{C}) + \Psi_{\text{vol}}(J)$$

Ψ_{vol} is simply a term that penalizes volume changes in the material ($J = 1$ corresponds to no volume change, while deviations from $J = 1$ signify changing volume). The simplest form of Ψ_{vol} is given by

$$\Psi_{\text{vol}} = \frac{1}{2}K(J-1)^2\,, \tag{4}$$

with K a bulk modulus parameter. When this form of Ψ_{vol} is used, the second Piola Kirchhoff stress can be obtained as

$$\mathbf{S} = 2\frac{\partial\hat{\Psi}(\mathbf{C})}{\partial\mathbf{C}} + K(J-1)J\mathbf{C}^{-1}. \tag{5}$$

The only task that remains ahead before we can model the behavior of a hyperelastic material is to specify a suitable form of $\hat{\Psi}$. $\hat{\Psi}$ has to satisfy a number of mathematical and physical constraints to be admissible. First and foremost, $\hat{\Psi}$ has to be *objective*. Simply put, the principle of objectivity states that the stress in the material must be independent of the frame of reference. There are two widely used methods of satisfying this criterion: 1) using SEDFs that only depend on the principal (distortional) stretches, $\hat{\lambda}_1, \hat{\lambda}_2, \hat{\lambda}_3$ (square roots of the eigenvalues of $\hat{\mathbf{C}}$) [47, 44], or 2) using SEDFs that only depend on the tensor invariants of $\hat{\mathbf{C}}$ [48].

Once a suitable form of $\hat{\Psi}$ is determined, one can use either one of the hypotheses of exactly incompressible hyperelasticity (Eq. (3)) or nearly incompressible hyperelasticity (Eq. (5)) depending on the application.

2.2. Principal stretch-based hyperelasticity

The most famous of the principal stretch-based models of hyperelasticity is perhaps the model proposed by Ogden originally for rubber [49]. This SEDF is widely and successfully used to model soft tissues that are isotropic, such as fibrin clots, adipose tissue, and brain tissue [50, 51, 52, 47]. The distortional SEDF in this model is given by

$$\hat{\Psi}(\hat{\lambda}_1, \hat{\lambda}_2, \hat{\lambda}_3) = \sum_{p=1}^{N} \frac{\mu_p}{\alpha_p}(\hat{\lambda}_1^{\alpha_p} + \hat{\lambda}_2^{\alpha_p} + \hat{\lambda}_3^{\alpha_p} - 3), \quad \mu_p\alpha_p > 0 \tag{6}$$

where μ_p and α_p, $p \in \{1, 2, ..., N\}$, are material parameters. As mentioned previously, when dealing with *nearly incompressible* problems, this distortional energy function is paired with a suitable volumetric energy function (such as the one in Eq. (4)) to obtain the full strain energy function.

It has been shown that this form of the SEDF satisfies the relevant physics-based constraints such as polyconvexity and thermodynamic consistency [53].

2.3. Invariant-based hyperelasticity

In invariant-based hyperelasticity the distortional SEDF depends only on the matrix invariants of $\hat{\mathbf{C}}$. The *principal invariants* of $\hat{\mathbf{C}}$ are given as

$$\hat{I}_1 = \mathrm{tr}\hat{\mathbf{C}} = \hat{C}_{11} + \hat{C}_{22} + \hat{C}_{33}$$
$$\hat{I}_2 = \frac{1}{2}(\hat{I}_1^2 - \mathrm{tr}\hat{\mathbf{C}}^2)$$

The third invariant, $\hat{I}_3 = \det \hat{\mathbf{C}}$, is irrelevant since the determinant of the isochoric part of $\mathbf{C}$ (i.e. $\hat{\mathbf{C}}$) is always equal to 1 by definition.

In addition to $\hat{I}_1, \hat{I}_2$, one can use a number of *direction-dependent* invariants to model *anisotropic* material behavior. The simplest of these is given as

$$\hat{I}_{4v} = \mathbf{v}_0 \cdot \hat{\mathbf{C}}\mathbf{v}_0$$

where $\mathbf{v}_0$ is a vector in the reference configuration and $\hat{I}_{4v}$ is the anisotropic invariant corresponding to $\mathbf{v}_0$ [54]. $\hat{I}_{4v}$ can also be interpreted as the square of the stretch of the material in the direction $\mathbf{v}_0$.

One of the most widely used invariant-based models of soft tissue hyperelasticity is known as the GOH model [55] (Named after the authors Gasser, Ogden and Holzapfel). In the GOH model, $\hat{\Psi}$ is given as

$$\hat{\Psi} = C_{10}(\hat{I}_1 - 3) + \frac{k_1}{2k_2} \sum_{i=4v,4w} \Big\{ \exp[k_2(\kappa \hat{I}_1 + (1 - 3\kappa)\hat{I}_i - 1)^2] - 1 \Big\} \qquad (7)$$

where $\hat{I}_{4v}$ and $\hat{I}_{4w}$ are anisotropic invariants pertaining to the material vectors $\mathbf{v}$ and $\mathbf{w}$, and C_{10}, k_1, k_2 and κ are material parameters. The GOH model is widely used because the exponential function captures nicely the strain-stiffening response of collagenous tissues [56, 57]. Many other examples of SEDF have been developed for specific tissues such as heart valves [58, 14], skin [13, 59], cartilage [60], and ligaments [61], to name a few [56].

2.4. Experimental characterization

To determine material parameters for hyperelastic models, uniaxial and biaxial tensile tests are common [20, 62]. Uniaxial tensile tests are only justified for isotropic or transversely isotropic materials such as adipose tissue and ligaments [63, 64]. Biaxial tests are adequate for thin tissues that operate physiologically under tension such as skin [20]. For bulk tissues such as myocardium, triaxial testing is the most appropriate [65]. These testing modes are usually paired with the assumption of homogeneous stress/strain fields. Increased accuracy during parameter identification can be achieved with inverse finite element methods and/or full-field strain measurements [64, 66].

3. Viscoelastic behavior

Viscoelasticity is an energy dissipation mechanism. The two most natural experiments or observations of viscoelastic behavior are creep and relaxation [67, 68]. When a viscoelastic tissue is stretched to a given deformation, the force required to maintain the deformation decreases over time, i.e. the material shows stress relaxation [67]. If a constant force is applied to a viscoelastic material, there will be an initial elastic deformation followed by strain increase or creep over time [68]. The notion of energy dissipation suggests that a good framework to describe viscoelasticity of soft tissue is within an energy framework, considering contributions to the free energy that come from the SEDF, as in hyperelasticity, as well as an elastic energy that can change over time [69, 70]. However, before arriving at the energy approach, other common alternatives are explained first [71]. Even though the theory of linear elasticity is not applicable to soft tissue, some aspects of linear elasticity, and in particular linear viscoelasticity, can be used in the large deformation regime. Thus, we first present the framework of quasi-linear viscoelasticity (QLV), before discussing its extension to the realm of fractional calculus. The energy approach is described afterwards.

3.1. Quasi-linear viscoelasticity

Fung introduced the concept of quasi-linear viscoelastic behavior for soft tissue [19]. As the name suggests, there are some aspects of this theory that resemble the linear viscoelastic models. The second Piola Kirchhoff stress can be expressed as a convolution integral of the instantaneous elastic stress $\mathbf{S}^e(t)$ and a relaxation function $G(t)$,

$$\boldsymbol{S}(t) = \int_0^t G(t-s)\frac{d\boldsymbol{S}^e}{ds}ds. \tag{8}$$

This is analogous to linear viscoelastic models, with the main difference that the elastic stress in eq. (8) can be a nonlinear function of the deformation, for instance any of the hyperelastic models for tissue described above, e.g. Eq. (7). The *linear* part of the name comes from the split of the stress and the relaxation function, which appears linearly in the convolution integral (8). For tissue, as introduced by Fung and refined by others, a good relaxation function is of the form [72],

$$G(t) = \frac{1 + \int_0^\infty S(\xi)e^{-t/\xi}d\xi}{1 + \int_0^\infty S(\xi)d\xi} \tag{9}$$

with $S(\tau)$ a relaxation spectrum of time constants, for example $S(\tau) = 1/\tau$, i.e. a constant relaxation spectrum [73]. In other words Eq. (9) integrates the contribution of a spectrum of relaxation times with exponential decay. Normalization is needed so that the stress is bound by the instantaneous elastic stress $\mathbf{S}^e$. Relaxation functions are not entirely arbitrary, they do need to satisfy certain physical principles and some intuition. For energy dissipation, $G(t)$ has to be a monotonically decreasing non-negative function. Additionally, if fading memory is desired, then the function has to be convex [74, 75]. One of the limitations of the approach is the choice of the relaxation function, which might be difficult to determine for soft tissue. Another limitation is the convolutional integral which requires integrating over the entire history of loading. This can become computationally expensive. An efficient numerical scheme is to consider only a finite expansion of exponential dissipation terms [76],

$$G(t) = \gamma_0 + \sum_{i=1}^{N} \gamma_i e^{\frac{-t}{\tau_i}} \tag{10}$$

where $\gamma_0 = 1$ such that the initial stress is $\mathbf{S}(0) = \mathbf{S}^e$ and γ_i are normalized moduli. For a given exponential decay function, internal variable $\mathbf{H}^{(i)}$ will be used to keep track of the stress in branch i,

$$\boldsymbol{H}^{(i)} = \int_0^t e^{\frac{-(t-s)}{\tau_i}} \frac{d\boldsymbol{S}^e}{ds}ds\,. \tag{11}$$

Adding up all the contributions to the stress from each of these viscoelastic branches, the total stress at time t is

$$\boldsymbol{S}(t) = \boldsymbol{S}^e(t) + \sum_{i=1}^{N} \gamma_i \boldsymbol{H}^{(i)}(t). \tag{12}$$

For a new time step $n+1$ corresponding to the time $t+\Delta t$, updating each of the internal variables $\mathbf{H}^{(i)}$ is needed to update the stress. Due to the nature of exponential functions, it can be verified that after some manipulation, the update of the internal variable has the form [76, 77],

$$\boldsymbol{H}^i_{n+1} = e^{\frac{-\Delta t}{\tau_i}} \boldsymbol{H}^i_n + \frac{1 - e^{\frac{-\Delta t}{\tau_i}}}{(\Delta t/\tau_i)} (\boldsymbol{S}^e_{n+1} - \boldsymbol{S}^e_n). \tag{13}$$

Thus, Eq. (13) updates all the internal variables, with the only unknown in Eq. (13) the new instantaneous elastic stress $\boldsymbol{S}^e_{n+1}$, since all the other information is just from the previous time step. The stress tensor$\boldsymbol{S}^e_{n+1}$, as mentioned before, can be any of the nonlinear hyperelastic models used in soft tissue model, e.g. the one defined in Eq. (7). For example, a viscoelastic framework for ligaments, adipose, and other soft tissues, based on the convolution of a relaxation function and an anisotropic strain energy function is developed in [61, 78, 79].

3.2. Fractional viscoelasticity

Recall the QLV framework, which relies on the convolutional integral of the relaxation function times the rate of change of the stress

$$\mathbf{S}(t) = \mathbf{S}^e(t) + \int_0^t G(t-s) \frac{d\mathbf{S}^e}{ds} ds\,. \tag{14}$$

As mentioned earlier, one of the main difficulties of the QLV framework is the numerical implementation, especially for non-exponential relaxation functions. From experimental observations, exponential decay is not a realistic description of tissue relaxation and, rather, power laws are expected [80, 81]. Thus, the QLV approach can be extended to a more general evolution equation involving fractional derivatives,

$$\mathbf{S}(t) = \mathbf{S}^e(t) + B_0 D^\alpha \mathbf{S}^e\,, \tag{15}$$

where D^α denotes the Caputo fractional derivative of order $\alpha \in (0,1)$ [82]

$$D^{\alpha}S = \frac{1}{\Gamma(1-\alpha)} \int_0^t (t-s)^{-\alpha} \dot{S} ds \,, \tag{16}$$

with $\Gamma(\circ)$ the Gamma function and $\dot{\circ}$ the integer order derivative of the function S. As can be seen from the convolution in Eq. (16), this model incorporates power law decay. The advantage of this approach is that, due to the inherent power-law behavior observed in tissues, the fractional derivative offers a very elegant and succinct description of the viscoelastic behavior with a much smaller number of parameters [81]. Unlike exponential decay approaches, which require a very large number of parameters (two per exponential decay branch), the fractional approach condenses the response to the fractional order α and a modulus B_0 [83]. Numerical implementation does require a Prony series expansion for memory efficiency of the convolutional integral. The Prony series might require several terms in the expansion, typically on the order of 12 internal variables are needed for the Prony series[84], but it should be emphasized that regardless of the Prony series, only two parameters are needed to represent the rich relaxation behavior [84].

3.3. Finite deformation non-equilibrium viscoelasticity

One limitation of QLV is that it is not necessarily compatible with large deformations far from thermodynamic equilibrium. Starting with the definition of the free energy it is possible to establish a robust theory for non-equilibrium finite viscoelasticity [70, 69]. The free energy is thus expressed

$$\Psi = \Psi^M_{EQ}(\mathbf{C}) + \Psi^F_{EQ}(\mathbf{C}) + \Psi^M_{NEQ}(\mathbf{C}^M_e) + \Psi^F_{NEQ}(\mathbf{C}^F_e) \tag{17}$$

with equilibrium (EQ) and non-equilibrium (NEQ) contributions. Furthermore, just as in the hyperelastic case, the energy can be attributed to an isotropic ground substance or matrix (M), and an anisotropic contribution from fiber reinforcements (F, usually collagen). Each of these four terms in (17) can have a very similar structure to the energies identified before, e.g. Eq. (7). Note also that the equilibrium energy depends on the total deformation $\mathbf{C}$. In contrast, the non-equilibrium deformation naturally has to be expressed in terms of internal variables that are used to keep track of the dissipation over time. In the QLV case the internal variables were the stresses $\mathbf{H}^{(i)}$. Here, the internal variables are kinematic. The total deformation gradient can be split into the elastic and inelastic contributions for the matrix and fiber

$$\mathbf{F} = \mathbf{F}_e^M \mathbf{F}_i^M = \mathbf{F}_e^F \mathbf{F}_i^F \,, \tag{18}$$

just as originally introduced for finite plasticity [85, 86]. The split of the deformation gradient leads to the corresponding deformation tensors $\mathbf{C} = \mathbf{F}^\top \mathbf{F}, \mathbf{C}_e = \mathbf{F}_e^\top \mathbf{F}_e, \mathbf{C}_i = \mathbf{F}_i^\top \mathbf{F}_i$. The combination of the multiplicative split of the deformation and the additive split of the energy has been successfully used to model a variety of soft tissue such as cardiovascular tissue, cornea, and skin [87, 88, 89]. The dissipation inequality leads to the following condition for the rate of change of the inelastic deformation [90]

$$-2\frac{\partial \Psi}{\partial \mathbf{C}_i^M} : \frac{1}{2}\dot{\mathbf{C}}_i^M - 2\frac{\partial \Psi}{\partial \mathbf{C}_i^F} : \frac{1}{2}\dot{\mathbf{C}}_i^F \geq 0 \,. \tag{19}$$

Alternatively, Eq. (19) can be turned into a requirement for the rate of change of the elastic deformation. Furthermore, requiring that both terms of Eq. (19) are satisfied independently, i.e. that the matrix and fiber parts independently satisfy positive energy dissipation, the elastic deformation of the matrix satisfies

$$-\tau_{NEQ}^M : \frac{1}{2}(\mathscr{L}\mathbf{b}_e^M)(\mathbf{b}_e^M)^{-1} \geq 0 \tag{20}$$

and a similar argument is done for the fiber part. In Eq. (20), the rate of change of the elastic deformation $\mathbf{b}_e$ is computed with the Lie derivative $\mathscr{L}$. Note that the energy dissipation involves the non-equilibrium Kirchhoff stress τ_{NEQ}, conjugate to $\mathbf{b}_e$. To close the system of equations, a rate equation is needed to drive the update of $\mathbf{b}_e$ or $\mathbf{C}_i$, depending on which one is used as the internal variable. A suitable method to drive the evolution of the internal variable is to introduce a dissipation potential Φ such that the rate of change of $\mathbf{b}_e$ follows

$$-\frac{1}{2}(\mathscr{L}\mathbf{b}_e^M)\mathbf{b}_e^{M\,-1} = \frac{\partial \Phi}{\partial \tau_{NEQ}^M} \,. \tag{21}$$

A sufficient requirement on Φ is that it should be convex with respect to τ_{NEQ} and $\Phi = 0$ when $\tau_{NEQ} = \mathbf{0}$. This is sufficient but not necessary [70].

A general dissipation potential that works well for a variety of tissues was proposed in [70],

$$\Phi_{RG} = \frac{1}{9\eta_V}(I_1^\tau)^2 + \frac{1}{3\eta_D}((I_1^\tau)^2 - 3I_2^\tau)\,, \tag{22}$$

where η_V, η_D are two dissipation time scales, and I_1^τ, I_2^τ are the first two invariants of the non-equilibrium stress τ_{NEQ}^M. For the anisotropic part, simpler dissipation potentials are common [90]

$$\left(\frac{\dot{\lambda}_i^F}{\lambda_i^F}\right) = \frac{1}{\eta_F}\tau_{NEQ}^F \tag{23}$$

where η_F is a positive parameter that represents the characteristics viscosity of the fiber, and τ_{NEQ}^F is the non-equilibrium Kirchhoff stress in the fiber.

3.4. Experimental characterization

As mentioned at the beginning of the section, two main experimental observations of viscoelasticity are creep and stress relaxation. Stress relaxation in particular is a popular testing method to determine parameters of viscoelastic response experimentally [52, 42, 91]. An important control variable during the experiments is consideration of strain rate [52, 92]. Other methods include indentation, in particular for highly hydrated tissues which are difficult to mount on uniaxial tension equipment such as brain [93, 94]. Cyclic loading can also be used to infer dynamic tissue properties [95].

4. Damage

Damage is another phenomenon that dissipates energy and reduces the apparent stiffness of a material with respect to its virgin state [96]. A classical treatment of damage is through the continuum damage mechanics framework [97]. The concept of damage in a material is associated with the nucleation of micro-cracks or voids in the material which reduce the stiffness without an apparent plastic deformation [96]. A natural framework for describing damage is to scale the virgin strain energy by a damage internal variable

$$\Psi = (1-d)\Psi_0\,, \tag{24}$$

where the notation Ψ_0 is for the undamaged or virgin strain energy, and d is the damage variable. Initially $d = 0$ and there is no damage. As damage progresses, up to $d = 1$, energy is dissipated. For $d = 1$ there is complete material degradation and failure. This scaling of the energy by a damage variable is actually the same approach to fracture mechanics with the phase-field method [98, 99]. There are other frameworks for modeling damage. For soft materials, the observation of the Mullins effect in rubbers resulted in pseudo-elastic frameworks to describe this behavior [100]. The Mullins effect in rubbers is the observation that when rubber is stretched to a given total deformation, returned to the initially undeformed state and loaded back again to the same maximum deformation as before, the stress-stretch response of the second loading cycle falls underneath the stress-stretch curve of the first loading cycle. Furthermore, the amount of damage depends on the maximum deformation only [101]. Because modeling of soft tissue mechanics follows closely the advances in rubber mechanics, many of the models for rubber damage have been applied to soft tissue [102, 103, 104, 105].

Following the energy approach from Eq. (24), the undamaged strain energy can still be modeled with any of the hyperelastic potentials as described in previous sections, e.g. Eq. (7). The stress is also obtained as before but with the scaling by the damage variable $\mathbf{S} = (1 - d)\mathbf{S}_0$. The dissipation inequality leads to an additional term that imposes a constraint on damage dissipation, namely

$$Y\dot{d} \geq 0 \tag{25}$$

where $Y = \partial\Psi/\partial d$ is the thermodynamic conjugate variable to the damage variable. In the case of Eq. (24), $Y = \Psi_0$, the undamaged strain energy is the driving force [97]. To link the damage evolution to the conjugate variable, one approach similar to the introduction of a dissipation potential in viscoelasticity, is a yield potential of the form $G(Y)$. If $G(Y)$ is convex and the evolution of damage is proportional to its derivative $\dot{d} \propto \partial G/\partial Y$, then Eq. (25) is satisfied. There is one important difference during damage compared to other dissipation mechanisms such as viscoelasticity. In the viscoelastic frameworks above, the internal variables can *recover*. Damage is modeled as an *irreversible* behavior, requiring an additional constraint. Introducing the damage history variable $r = \max_{s\in(0,t]}(r_0, Y)$, with r_0 the initial damage threshold. In other words, r keeps track of the maximum value of the thermodynamic conjugate variable over the loading history. Thus, rather than

evaluating the yield potential $G(Y)$, the yield criterion is actually given by

$$g(Y, r) = G(Y) - G(r)\,. \tag{26}$$

In other words, Eq. (26) is used to keep track of whether or not the deformation exceeds the previous level of damage. Damage evolution is then given by the rate equation

$$\dot{d} = \dot{\mu}\frac{\partial g(Y, r)}{\partial Y} \tag{27}$$

with $\dot{\mu} \geq 0$ a damage consistency parameter to ensure irreversible damage via the Kuhn-Tucker relations

$$\dot{\mu} \geq 0, \quad g(Y, r) \leq 0, \quad \dot{\mu} g(Y, r) = 0. \tag{28}$$

Eq. (28) imposes a one-sided constraint so that $\dot{d} \geq 0$, i.e. irreversibility of the damage process. The only thing to close the system of equations is the yield potential. In [97], the yield criteria is $\bar{\tau} = \sqrt{\Psi_0}$. For soft tissue, different yield criteria, or equivalently, different $d(\Psi_0)$ have been proposed [106, 78, 107, 108]. For example, an exponential-type damage model developed for tissues is of the form [108],

$$d(Y) = 1 - \exp\left(\frac{\beta\, Y}{\alpha}\right)\,, \tag{29}$$

with α, β material parameters. Another proposed damage function for collagen fibers is of the form [106]

$$d(Y) = 1 - \frac{1 - \exp(\mu[G(Y) - \alpha])}{1 - \exp(\mu[\beta - \alpha])} \tag{30}$$

with μ, α, β material parameters, and $G(Y)$ a monotonic function to keep track of the damage yield surface, for instance $\sqrt{\Psi_0}$ as in [97].

Experimental characterization of damage behavior can be done via cyclic loading at progressively higher deformation [63, 109, 52].

5. Multi-phasic behavior

Tissues are made up of multiple constituents. A ground substance of different proteins is usually assumed as a soft isotropic material, with collagen and elastic fibers treated as fiber reinforcements with much greater

stiffness [78, 54]. Under these considerations, in the sections above, the tissue is modeled as a solid, with microstructure approaches used to distinguish between the contribution of each constituent. In some tissues, however, it is not reasonable to assume the material behaves only as a solid. Instead, a mixture of solid and fluid phases is needed, just like in other soft material systems e.g. hydrogels or saturated soils [110, 111]. Following the saturated poroleasticity theories as applied to soft tissue [24], we start by modifying the balance equations introduced above. Momentum balance leads to a two field equation. First, linear momentum balance states

$$\nabla \cdot \boldsymbol{\sigma} = \mathbf{0}, \tag{31}$$

with $\boldsymbol{\sigma}$ the stress tensor which now depends on two fields, the displacement of the solid $\mathbf{u}$, and a fluid pressure field p_f, such that the total stress is decomposed as

$$\boldsymbol{\sigma} = -p_f \boldsymbol{I} + \boldsymbol{\sigma}^{\mathbf{e}} \,. \tag{32}$$

In Eq. (32), the elastic stress $\boldsymbol{\sigma}^e$ is, just as before, computed from the hyperelastic or viscoelastic models already established above. The introduction of the new field p_f implies the need for another balance equation. Indeed, mass balance of the fluid, due to its motion relative to the solid, leads to

$$\nabla \cdot \boldsymbol{v} = 0 \,, \tag{33}$$

where the velocity $\boldsymbol{v}$ of the fluid relative to the solid has been introduced. The relative fluid velocity is coupled to the pressure field via Darcy's law

$$\boldsymbol{w} = -\boldsymbol{k} \cdot \nabla p_f \,, \tag{34}$$

with $\boldsymbol{k}$ the hydraulic conductivity tensor [112]. In principle, the Eqs. (31)-(34) close the system of equations (given a strain energy to compute the elastic stress). One important consideration is that the deformation of the solid actually leads to changes in hydraulic conductivity, and the tensor $\boldsymbol{k}$ should not be treated as a constant. Intuitively, as pores are closed when the material is compressed, the conductivity should decrease, and vice-versa. Several coupling models between the fluid transport and the solid deformation have been introduced, with the Holmes-Mow model a popular one for cartilage and subcutaneous tissue [77, 113, 114],

$$k(J) = k_0 \left(\frac{J - \varphi_r^s}{1 - \varphi_r^s} \right)^{\alpha} e^{\frac{1}{2} M (J^2 - 1)}, \tag{35}$$

where k_0 is the initial permeability, φ_r^s is the initial solid volume fraction, α and M are two material parameters, and $J = \det \mathbf{F}$ is the volume change.

Generalizations of the hydraulic conductivity dependence on tissue anisotropy and anisotropic deformations has also been explored, particularly for cartilage [115, 60].

In addition to cartilage, poroelasticity is also central to the behavior of subcutaneous tissue, particularly during drug delivery [27, 116, 117]. Recently, poroelastic frameworks have been applied to brain tissues [118, 119], lung [120, 121], among other organs [59, 93].

Experimentally, multi-phasic behavior can be characterized through confined compression [24]. During confined compression, fluid is forced out of the tissue, offering an opportunity to determine the transport properties (hydraulic conductivity), in addition to the solid phase properties. Alternatively, a combination of tests can be done to separately determine fluid transport parameters and elastic stress parameters [122]. Fluid exchange between tissue and a fluid bath can also be controlled by changing the osmolarity of the bath, offering another avenue to determine multi-phasic properties [59]. Lastly, indentation is also a suitable method for determination of biphasic properties [123].

6. Active materials

Many soft tissues have a mechanical support role, but we also have tissues in our bodies that are able to generate motion, namely muscle tissue [8]. There are three main kinds of muscle tissue: skeletal, cardiac, and smooth [124]. In addition, even tissues that traditionally have a support role, are under some amount of residual tension that ultimately can be explained from cellular activity at the microscale: fibroblasts, the most common connective tissue cell type, pulling on the extracellular matrix (ECM) [35]. Therefore, some models explaining residual stress in soft tissues that are not regarded as *active* as muscle do still consider some active stress contribution [125]. Muscle and active forces from fibroblasts are very different at the microscale, but at the continuum scale they can be similarly incorporated. The main method is to consider the total stress as a combination of passive and active components

$$\boldsymbol{\sigma} = \boldsymbol{\sigma}^e + \boldsymbol{\sigma}^a \tag{36}$$

where $\boldsymbol{\sigma}^a$ denotes an active component that does not appear from a strain energy density function (although it can also be framed in an energy framework [126]). The split can be pulled back to the reference configuration to obtain either the nominal stress $\mathbf{P}$ or the second Piola Kirchhoff stress $\mathbf{S}$. However, unlike the passive or elastic stress, the active stress is naturally associated with the current configuration,

$$\boldsymbol{\sigma}^a = t^a \mathbf{a} \otimes \mathbf{a} \tag{37}$$

with the active traction t^a primarily along the current fiber direction $\mathbf{a}$ in the deformed configuration. Eq. (37) thus describes active forces primarily along fiber direction. For skeletal and cardiac muscle there are preferred alignment of muscle fibers that drive the motion along a particular orientation and Eq. (37) is a good model of active tension. However, if there is no preferred fiber direction, or if there is some dispersion in the fiber orientation, then a structural tensor accounting for dispersion can be used instead of $\mathbf{a} \otimes \mathbf{a}$, or a micro-sphere approach [35, 127]. While the anatomy and biology of different tissues is not covered in detail in this review, it is worth mentioning that for muscle tissue, the main active unit is called the sarcomere, a contractile unit on the order of $1 - 3\mu$m. Sarcomeres have overlapping acting a myosin filaments. The myosin filaments have protrusions or heads that form transient bridges to the actin filaments, Upon electrical activation, the myosin heads generate torque that moves the actin and myosin filaments passed each other, generating contraction. Models of sarcomere biophysics explain the dynamics of force generation [128]. Sarcomeres assemble into myofibrils, which then form muscle fibers. Muscle fibers can assemble into fascicles, which then compose the entire muscle [28]. Due to the high degree of alignment, it is natural to express the active force in the direction of the fiber $\mathbf{a}$. In the heart, the fibers are much shorter than in skeletal muscle, but they still do show a preferential alignment, although, compared to skeletal muscle, the fibers in the heart show much greater variation from point to point, that is, the vector field $\mathbf{a}(\mathbf{x})$ is highly heterogeneous albeit predictable. For instance, heart muscle fibers have a helicoidal arrangement in the heart, with the outer surface having fibers oriented -70^o with respect to the vertical axis (from the bottom of the heart to the top), and the inner surface having alignment $+90^o$ [129]. Smooth muscle does not have a strong fiber

alignment and produces isotropic or transversely isotropic stress that can be captured with a suitable fiber distribution [130, 131]. Smooth muscle can be found in the walls of arteries, along the airways, or in the uterus [132, 133]. Irrespective of the split of the stress into passive (elastic) and active parts, the equilibrium equation is the same as before, $\nabla \cdot \boldsymbol{\sigma} = 0$.

The active traction t^a is not constant, it is driven by electrical activity. Because of this, active tissue behavior requires the solution of one more problem describing electrical activity [134]. The form of the electro-physiology problem is that of reaction diffusion system

$$\dot{\Phi} - \nabla \cdot \mathbf{q} = f_\Phi \tag{38}$$

where Φ is the electrical potential, $\mathbf{q}$ is the electrical flux, and f_Φ is a source term. The flux follows standard dissipation

$$\mathbf{q} = \mathbf{D}\nabla\Phi \tag{39}$$

with conductivity tensor $\mathbf{D}$. Muscle is assumed to obey a kinetic relation between electrical activation and maximum loading. Even if there is some electrical signal, the response is not instantaneous. A popular model by Nash and Panfilov states [135],

$$\dot{t}^a = \epsilon(\Phi)\left(k_a(\Phi - \Phi_r) - t^a\right) \tag{40}$$

where the active traction t^a increases in time until it reaches the maximum value $k_a(\Phi - \Phi_r)$. This maximum value states that when the muscle is actively contracting it will exert a traction proportional to the potential difference between the current potential Φ and a resting potential Φ_r. The function $\epsilon(\Phi)$ functions as a gating function, i.e. a Heaviside function which determines at which threshold of the potential Φ the muscle will actually contract.

Thus, from Eq. (40) we get the coupling between the electrical potential and the active traction. Eq. (38) provides the transport law for the electrical potential, with a flux proportional to the gradient through an anisotropic conductivity tensor with preference for the action potential propagation along the fibers. The last part of the model we have to define is actually the one with the richest history, the source term f_ϕ. This source term is what determines if the cells can have oscillatory response and self-excitation [136]. The excitation f_Φ can have a purely electrical term and also a stretch-induced

opening of ion channels in the cell leading to a change in the electrical potential $f_\Phi = f_\Phi^e + f_\Phi^m$. The purely electrical part can be modeled based on [137],

$$f_\Phi^e = c\Phi(\Phi - \alpha)(1 - \Phi) - r\Phi \tag{41}$$

where r is termed the recovery variable, and c and α are parameters. The recovery variable r, itself obeys a differential equation dependent on Φ, which is what allows for the rich dynamics. One possible coupling leading to oscillations of the action potential is [137]

$$\dot{r} = \left[\gamma + \frac{\mu_1 r}{\mu_2 + \Phi}\right] \left[-r - c\Phi(\Phi - b)\right], \tag{42}$$

with $\gamma, \mu_1, \mu_2, c, b$ material parameters. The model introduced thus far to describe cardiac electrophysiology is a relatively simplified model considering a single field for the potential and single state variable for the source term. More mechanistic models keep track of concentration of different ions and their transport in the heart tissue coupled to the electrical potential [138, 129]. Significant amount of work has also been made to bridge models of single cells to the tissue level Eq. (38) again through the source term [139, 140].

7. Growth, remodeling, wound healing

The most unique aspect of soft materials is perhaps their ability to adapt over time to mechanical input by adding mass, changing their shape, or changing their composition and mechanical properties [33]. The process by which cells translate mechanical signals from outside of the cell to chemical reactions and eventually gene expression and cell activity, is called mechanotransduction [141]. The field of study of how cells sense and react to mechanical load and modify their ECM is called mechanobiology [142]. The literature distinguishes between two main forms of adaptation: growth is commonly associated with a change in mass [36]; remodeling is associated with a change in mechanical properties due to ECM structure changes [125].

7.1. Growth

There are two main theories to model growth, a kinematic one and one based on reactive mixtures [34, 36].

The kinematic approach to model growth follows the multiplicative split of the deformation gradient into elastic and growth contributions similar to plasticity [143]

$$\mathbf{F} = \mathbf{F}^e\mathbf{F}^g \tag{43}$$

Again, similar to plasticity, it is assumed that $\mathbf{F}^e$ contains the deformation from an infinitesimal stress-free volume to the current state. Because the tensor $\mathbf{F}^e$ restores an infinitesimal volume to a stress free configuration, the strain energy is only a function of this deformation $\Psi(\mathbf{F}^e)$. Any of the hyperelastic strain energy functions defined so far can be used to model this response. Unlike traditional plasticity, $\mathbf{F}^g$ does not measure a defect motion (e.g. dislocations), but rather addition of mass [144]. In fact $J^g = \det(\mathbf{F}^g)$ is the volume change due to a change in mass at constant stress-free density ρ_0. Mechanical equilibrium is the same as always $\nabla \cdot \boldsymbol{\sigma} = 0$. The multiplicative split introduces an internal variable in $\mathbf{F}^g$, and thus we need an evolution equation to specify its rate of change $\dot{\mathbf{F}}^g$. Further assumptions regarding the growth tensor are commonly introduced. For instance, for isotropic growth, i.e. mass is added in all directions equally, the growth tensor can be expressed with a single scalar field ϑ^g,

$$\mathbf{F}^g = \vartheta\mathbf{I}\,, \tag{44}$$

whereas for growth in a particular plane defined by a normal $\mathbf{N}$ or growth along a fiber direction $\mathbf{a}_0$, the growth tensor can also be reduced to scalar fields [145]

$$\begin{aligned}\mathbf{F}^g &= \vartheta^g\mathbf{I} + (1-\vartheta^g)\mathbf{N}\otimes\mathbf{N}\\ \mathbf{F}^g &= \mathbf{I} + (\vartheta^g - 1)\mathbf{a}_0\otimes\mathbf{a}_0\,.\end{aligned}$$

Through the definition of the growth tensor in terms of a scalar field, then the evolution of growth can be done with a rate equation for a scalar rather than a tensor field, avoiding issues with objectivity and frame indifference. The rate of change of the internal variable ϑ^g is usually coupled to mechanical input but this is not always the case. The growth can be morphogenetic, for example during development, in which case it is an uncoupled model from mechanical input $\dot{\vartheta}^g = \alpha$. Constant growth rate means for example linear growth $\vartheta^g = \alpha t + 1$ with the assumption of initial condition $\vartheta^g(0) =$

1. Linear growth is observed in some system which grow relatively slowly [146]. However, many biological systems are governed by cell population dynamics with exponential growth. In such case the growth would have an exponential increase. To avoid unbounded growth, logistic growth models can be used in order to saturate the growth response due to, for instance, nutrient limitations [147].

The most interesting observations regarding tissue growth is when this process is tightly coupled to mechanical input. The most intuitive example is the build up muscle with exercise [148]. An example of maladaptation is thickening of the heart due to hypertension [149]. To couple growth to mechanical cues there are two main alternatives: to couple to stress or to strain. Either one of these metrics can lead to an effective constitutive model for $\dot{\vartheta}^g$. For example, coupling to stress [148]

$$\dot{\vartheta}^g = \frac{1}{\tau_g}\left[\frac{\vartheta^g_{\max} - \vartheta^g}{\vartheta^g_{\max} - 1}\right](\mathrm{tr}\mathbf{M}^e - M^e_{\mathrm{crit}}) \tag{45}$$

with τ_g a characteristic time constant for the growth process, the parameter $\vartheta^g_{\max}$ preventing unbound growth and serving the role of logistic terms that control maximum density of cell populations, and the parameter M^e_{crit} a critical stress triggering growth, i.e. a target or homeostatic stress. The tensor $\mathbf{M}^e$ is the Mandel stress $\mathbf{M}^e = \mathbf{C}^e\mathbf{S}^e$ with $\mathbf{C}^e = \mathbf{F}^{e\top}\mathbf{F}^e$ the elastic right Cauchy Green deformation tensor, and $\mathbf{S}^e = \mathbf{F}^g\mathbf{S}\mathbf{F}^{g\top}$ the second Piola Kirchoff stress pushed to the intermediate configuration. The choice of Mandel stress is because it is work-conjugate to the growth velocity gradient $\mathbf{L}^g = \dot{\mathbf{F}}^g\mathbf{F}^{g-1}$, and a proper relationship between this stress measure and the growth velocity gradient is needed for energy dissipation [105].

In some systems, it is convenient to express the growth rate in terms of elastic kinematic variables. For example for skin, in the context of tissue expansion, growth rate can be coupled to elastic area changes [150, 151]. Tissue expansion is a technique in reconstructive surgery to grow new skin in situ with properties similar to adjacent tissue [152]. In tissue expansion, a balloon-like device is inserted subcutaneously and inflated gradually with saline solution, stretching the skin and triggering its growth [153]. Intuitively, stretching the skin chronically beyond a physiological state induces growth of new skin. This happens naturally in pregnant women and when we gain weight. Clinically, the tissue expansion process is kinematically driven. The surgeons control the volume of inflation [154, 155]. Becuase of the kinematic control, the growth rate can be expressed as a function of the elastic

deformation [150]

$$\dot{\vartheta}^g = k_g(\vartheta^e - \vartheta^g_{\text{crit}}) \tag{46}$$

with the elastic area change $\vartheta^e = ||(\text{cof}\mathbf{F}^e)\mathbf{N}||$.

Driven by stress or strain, the growth formulations introduced so far remain largely phenomenological. This is because they ignore the cellular process of mechanotransduction. A more detailed description of the growth process is through reactive mixtures [34, 156]. In this framework, the focus is on the constituents that make up the tissue. For instance, keeping track of mass fractions of collagen, elastin, GAG proteins, etc [34, 157, 158].The mass fractions of different constituents are denoted ρ_i, which satisfy a joint mass transport equation

$$\dot{\rho}_i + \nabla \cdot (\mathbf{v}_i \rho_i) = m_i \,, \tag{47}$$

where $\mathbf{v}_i$ is the velocity of constituent i, and m_i the mass production rate of each constituent. The m_i can be functions of the different ρ_i, specifying reactions or conversions between different species.

The linear momentum balance of the mixture is the standard equilibrium equation, $\nabla \cdot \boldsymbol{\sigma} = \mathbf{0}$, but with the stress being a sum of the stress from each constituent

$$\sigma = \sum \sigma_i \,. \tag{48}$$

There is a constraint equation that relates the momentum exchange between different constituents

$$\sum (\mathbf{p}_i + m_i \mathbf{v}_i) = \mathbf{0} \,, \tag{49}$$

where $\mathbf{p}_i$ is the momentum exchange between constituent i and all other constituents [159]. The last part of the theory in order to encode either residual stress or stress relaxation due to growth is that new materials might be placed under some pre-tension by cells. The deformation of each individual constituent needs to be computed with respect to its own stress-free or *natural* configuration [160],

$$\mathbf{F}^{\text{t}}_i = \mathbf{F}\, \mathbf{F}^{\text{n}-1}_i\, \mathbf{G}_i \,, \tag{50}$$

with $\mathbf{F}^t_i$ the total deformation of constituent i at time t, $\mathbf{F}$ the deformation gradient with respect to some specified reference state, $\mathbf{F}^{n-1}_i$ the deformation

between the reference state and the state of the solid when the material i was deposited, and $\mathbf{G}_i$ the pre-tension of material i at the time it was deposited. Even when no pre-strain is assumed at the time of material deposition $\mathbf{G}_i = \mathbf{I}$, growth or residual stress can occur if there is some deformation $\mathbf{F} \neq \mathbf{I}$ and materials are deposited and degraded continuously in time.

While more detailed, mixture theory still uses phenomenological descriptions such as a homeostatic stress or a state of pre-tension in newly deposited material $\mathbf{G}_i$ [161]. One problem with the mixture theory approach is computational cost [162]. Although, with some assumptions, computational efficiency can be improved [163].

Recent efforts have focused on removing phenomenological assumptions in favor of even more detailed coupling to the cell scale, through multiscale models [164, 35]. Intermediate solutions between multi-scale model and purely phenomenological is to develop homogenized theories akin to what is done in micromechanics, for example [165].

7.2. Tissue remodeling

Remodeling is usually treated as a change in properties of the tissue without changing mass. For example, fiber reorientation is a classical example of remodeling [125]. By fiber reorientation it is meant here a permanent change in the fiber orientation at the stress-free state, as opposed to reorientation of fibers due to deformation [166]. The main assumption is that fibers tend to align themselves to the eigenvectors of the deformation tensor [167]. Given fibers initially in the direction $\mathbf{a}_0$, their orientation in the reference configuration evolves in time according to [168]

$$\dot{\mathbf{a}}_0 = \lambda_1 \left(\frac{2\pi \dot{\phi}^+}{\tau_\omega} \right) (\mathbf{I} - \mathbf{a}_0 \otimes \mathbf{a}_0)\mathbf{e}_1 \,, \tag{51}$$

where $\lambda_1, \mathbf{e}_1$ are the largest eigenvalue and corresponding eigenvector. Eq. (51) shows that alignment is in the direction of the eigenvector $\mathbf{e}_1$ proportional to the stretch λ_1 but also proportional to the rate of collagen remodeling $\dot{\phi}^+$ scaled by a characteristic time τ_ω. Reorientation can be applied independently to a collection of fibers in a micro-sphere approach. Alternatively, an efficient way of characterizing re-orientation of a fiber distributions is to define an evolution equation for fiber dispersion [169]

$$\dot{\kappa} = \frac{\dot{\phi}^+}{\tau_\kappa} \left(\frac{1}{3} \frac{\lambda_2^{\gamma_\kappa}}{\lambda_1^{\gamma_\kappa}} - \kappa \right) \tag{52}$$

which is also proportional to collagen turnover rate scaled by a possibly different time constant τ_κ, and tending toward the ratio of the first two eigenvalues with a power law parameterized by γ_κ. If the first two principal eigenvalues become equal then at least there is a plane of loading in which the deformation is equi-biaxial, in which case the fiber dispersion tends toward a uniform dispersion $\kappa \to 1/3$. In the case of uniaxial tension the dispersion would show trend $\kappa \to (1/3)(1/\lambda^{3\gamma_k/2}) \to 0$ as $\lambda \to \infty$.

Although more computationally expensive, a more mechanistic model is based on tracking individual fibers. For instance in [170, 171], deposition and removal of indidividual fibers in different orientations is used to keep track of the evolving fiber orientation distribution.

7.3. Wound healing

The equations used in wound healing modeling are almost the same as already introduced above for growth and remodeling [172]. The reasoning to split wound healing as a separate sub-section comes from the need to couple the mechanical changes to biological field variables. In the previous sub-sections for growth and remodeling, the evolution equations are coupled directly to mechanical fields such as strain or stress. Wound healing, on the other hand, involves a well-regulated cascade of cellular signaling that culminates in new tissue creation out of an initial fibrin clot [173]. Such complex process is not achievable without a control program, beyond a direct coupling to the mechanical fields. Thus, even if the emphasis here is on mechanics of soft tissue, insights on how tissue heals can guide self-healing of synthetic materials in the near future. The biology control program can be thought of as a blueprint for how a control system would look like for rebuilding engineered materials autonomously.

The central control in wound healing is given by cell populations which have reaction-diffusion with logistic growth and chemotaxis [173]. Mass balance is sought

$$\dot{\rho} = \nabla \cdot \mathbf{Q}_\rho + s_\rho \tag{53}$$

where ρ denotes a cell population. At least one cell population is needed to describe wound healing. Fibroblasts are the key cell type that rebuilds connective tissue [174, 175]. Other cell types in wound healing are epithelial cells, for example kerationocytes in the epidermis [176]. Additional cell types of interest are inflammation-related, e.g. macrophages or neutrophils [177,

178]. In Eq. (53), $\mathbf{Q}_\rho$ is the flux and s_ρ is the source. The flux is further defined as

$$\mathbf{Q}_\rho = -D_\rho(\phi, c)\nabla\rho + D_{\rho,c}\nabla c \tag{54}$$

where the term proportional to $\nabla\rho$ is a diffusion-type term with diffusion coefficient $D_\rho(\phi, c)$ where it is now implied that this diffusion coefficient, related to cell motility, has to be coupled to other signals such as collagen ϕ and cytokines c. For instance, increasing collagen mass fraction can favor cell motility and thus effective diffusivity [169] . The second term in Eq. (54) is a chemotaxis term, an advection-type term that promotes cell motion toward gradients of the chemical species c [179]. Here it can be seen already that to drive the action of cell types ρ to do the healing process, at least one initiator signal c is needed. When a tissue is injured, blood coagulates through a chemical process involving thrombin and fibrin [180]. Platelets from the blood get trapped in the wound site, undergo apoptosis, and release chemical signals that trigger the wound healing program [181]. At least this signal is needed in a mathematical modeling framework of wound healing.

The cytokine concentration satisfies standard advection-diffusion transport equations

$$\dot{c} = \nabla \cdot \mathbf{Q}_c + s_c\,, \tag{55}$$

similar to the cell population, but with flux just due to diffusion

$$\mathbf{Q}_c = -D_c\nabla c\,. \tag{56}$$

To complete the basic control, the source terms need to be defined. For the cells, logistic growth is assumed

$$s_\rho = \left(p_\rho + p_{\rho,c}\frac{c}{K_{\rho,c}+c} + p_{\rho,e}H(I^e)\right)\left(1 - \frac{\rho}{K_{\rho\rho}}\right)\rho - d_\rho\rho \tag{57}$$

where the parameters $p_\rho, p_{\rho,c}, p_{\rho,e}$ are for proliferation, with a saturation term $K_{\rho,c}$ which prevents unbounded sensitivity of the cell proliferation with respect to the chemical signal, while the saturation term $K_{\rho\rho}$ prevents unbounded cell population growth. The decay rate is d_ρ. Overall the logistic growth states that cells will proliferate with initial exponential growth which is slowed down by the term $1 - \rho/K_{\rho\rho}$ as ρ approaches the saturation value. The cytokine term is a boost on proliferation with saturation response as the cytokine concentration goes to $K_{\rho,c}$. There is one additional coupling

term which looks similar to the cytokine-induced proliferation. The production term $p_{\rho,e}$, denotes mechanobiology coupling, i.e. induced proliferation in response to mechanical cues captured through the mechanobiology function $H(I^e)$, described later.

The chemical concentration has a production linked back to the cell density:

$$s_c = (p_{c,\rho} c + p_{c,e} H(I^e)) \left(\frac{\rho}{K_{c,c} + c} \right) - d_c c \,, \tag{58}$$

the production by cells has a base rate of $p_{c,\rho}$ and a mechanobiology induced rate $p_{c,e}$ with saturation $K_{c,c}$ and decay rate d_c. This basic control system ensures that an initial signal in the wound given by spike in the chemical c leads to a recruitment of cells from the surrounding tissue into the wound. The chemical control is supplemented by the mechanobiological control $H(I^e)$ in terms of some invariant of the deformation I^e that can be sensed by cells, either strain or a stress quantity (just as described in the growth formulations) [172].

Finally, the coupling between this simple feedback control program and the evolution of the tissue mechanics is needed. The coupling occurs in the processes described already above: active stress, permanent deformation, remodeling. For instance the cell density can contribute to a change in mass fraction of the collagen

$$\dot{\phi} = \left(p_\phi + p_{\phi,c} \frac{c}{K_{\phi,c} + c} + p_{\phi_e} H(I^e) \right) \left(\frac{\rho}{K_{\phi,\phi} + \phi} \right) - (d_\phi + c\rho d_{\phi,c})\phi \,, \tag{59}$$

with base rate p_ϕ, cytokine rate $p_{\phi,c}$, mechanobiological rate $p_{\phi e}$. Saturation in production by the chemical is through the parameter $K_{\phi,c}$, while saturation due to increased density of collagen itself is through $K_{\phi,\phi}$. Collagen is produced by fibroblast cells ρ and decays naturally at a rate d_ϕ but also shows increased turnover in the presence of the chemokine with a rate $d_{\phi,c}$.

The plastic deformation rate and remodeling of the fiber orientation is the same as previously introduced. Finally, the system is closed by defining the feedback between the mechanics and the cell action in the mechanobiology sensing term

$$H(I^e) = \frac{1}{1 + \exp(-\gamma_e (I^e - \vartheta^e))} \,, \tag{60}$$

with parameters γ_e, ϑ^e. Other models of mechanobiology can be used, with more detailed description of cell adhesion and cell-ECM interface [165, 35].

8. Emerging focus: data-driven modeling

Most tools, both experimental and computational, are either very powerful or very versatile, but not both. Tools that perform very well on a given task do so because they have been custom-made for that task, with the drawback that their use is limited to that specific task. On the other hand, tools that can handle a large variety of tasks typically do not perform exceptionally well on any of them. Machine learning in computational mechanics is changing this view, by enabling unparalleled flexibility to model complex tissue behavior, all while keeping a very similar array of linear algebra operations with some nonlinear filters. Machine learning offers a variety of tools for constitutive modeling that are extremely powerful and yet flexible enough to be applied to a vast number of tissues, including elastic and inelastic response.

In constitutive modeling of soft tissue, the macroscopic culminations of all the processes and interactions that take place at the microscopic scale in a tissue under mechanical loading are abstracted in terms of a few mathematical descriptors. Traditionally, these mathematical models are developed by observing the general characteristic behaviors of a material, establishing an appropriate theoretical framework and identifying specific functional forms of the constitutive relation [182]. However, research from the past decade shows that data-driven methods can largely automate this process and deliver better performance than human-made models. This is not a surprising outcome, as representing such a sophisticated set of processes requires highly expressive mathematical models, and machine learning methods such as neural networks are famously known as *universal* approximators [183].

In hyperelasticity this abstraction is usually in the form of the strain energy density function (SEDF) (See (1)). The SEDF is a potential function that accounts for the way in which a material stores external work as elastic energy, and releases it upon unloading. A large number of closed-form SEDFs similar to (6) and (7) are proposed in the literature [184], and yet, there is no consensus on the choice of a material model, even for a specific material like skin [185]. This is largely due to the closed-form nature of such models, which inhibits their flexibility. Machine learning-based SEDFs have been

shown to capture mechanical behavior better than closed-form models for soft tissues from multiple species [186, 187].

Recently, data-driven models of hyperelasticity have been proposed that satisfy physics-based constraints such as polyconvexity by design. This characteristic enables these models to learn material response better with a small amount of training data, avoid overfitting, and extrapolate beyond the training region. Polyconvexity is a criterion for existence of energy minimizers in elasticity [188] and imposition of this criterion also helps with the numerical stability of the models in Newton-type solvers (such as in most finite element method packages) [189]. Polyconvex data-driven SEDFs have been constructed from neural ordinary differential equations [190] and input convex neural networks [191]. Some other studies leverage the findings from the history of constitutive material modeling in machine learning algorithms to conduct automated systems identification [192, 193]. Irrespective of the approach, most polyconvex data-driven models can learn material behavior extremely well, while displaying reasonable extrapolation capacity at the same time [194].

Data-driven modeling of inelastic behavior such as viscoelasticity and damage shows a similar pattern. Over the years, various approaches for modeling viscoelastic behavior have been proposed that range from simple black box models with no incorporated physical knowledge to highly interpretable data-driven frameworks where the relevant physical constraints are satisfied a priori [195]. For example, in [196], viscoelastic behavior of materials under cyclic loading is learned in the frequency domain by a data-driven model. The authors of [197] use a neural networks to learn the relationship between stress and strain increments. More recently, the predominant approach to modeling viscoelasticity has consisted of learning physics-constrained SEDFs and dissipation potentials within the theory of nonlinear viscoelasticity [89, 198, 199]. In parallel to purely data-driven approaches, some studies have focused on identifying the governing viscoelastic law from a library of existing constitutive forms [200, 201]. Similarly, damage in soft materials can be modeled using a variety of data-driven methods [202, 203].

Multiscale modeling is another area of soft tissue mechanics that stands to benefit significantly from the introduction of data-driven methods. Multiscale modeling refers to the analysis of material response at large scales (macroscale) by considering the behavior from smaller scales (microscale) [204]. The most common approach for multiscale analysis of heterogeneous materials is the FE^2 method [205], which involves performing finite element

analysis on a representative volume element (RVE) of the microscale for each point in the macroscale. FE^2 is an extremely costly analysis method, and a popular method for accelerating multiscale analysis is to learn and predict RVE behavior using artificial neural networks, in a process known as surrogate modeling [206, 207]. Once the artificial neural networks have been trained with sufficient RVE data, the microscale analysis takes insignificant amount of time as it only involves a single forward-pass of the neural network. For example, in [208] a fully connected neural network (FCNN) was trained with a large dataset of discrete fiber network RVEs and used to predict the mechanical behavior of biopolymer gels at the macroscale. In [209], the homogenized response of cubic lattice metamaterials is represented by artificial neural networks, and in [210] neural networks are used to learn the yield function of foams after training with RVE data. In [211], the authors develop an efficient data collection scheme which minimizes the number of microscale simulations required. The method is applied to a fiber reinforced composite with a highly nonlinear mechanical behavior.

In summary, while sticking to the fundamental continuum mechanics theories outlined here, machine learning methods are uniquely powerful to eliminate the need for closed-form constitutive equations. In particular, the role of data-driven methods to connect multiple types of data (microstructure information and macroscale response for instance) cannot be understated. An active research effort is to increase interpretability of data-driven frameworks [212]. Another important focus area of research today is generative artificial intelligence and uncertainty analysis in the context of soft tissue modeling [213].

9. Outlook

Soft tissues are unique with respect to other engineered materials. They have extreme mechanical behavior that cannot be described with linear theories. The starting point in this chapter was hyperelasticity, in order to first of all account for the large deformation regime in which all soft tissues operate. We built in complexity from there because soft tissues show a variety of physical phenomena such as viscoelastic energy dissipation and damage energy dissipation. Tissues are hydrated and sometimes the fluid flow with respect to the solid matrix is important, for instance in cartilage biomechanics or subcutaneous drug delivery. Therefore, we also covered core aspects of multiphasic theory. One of the most unique aspects of tissues is their ability

to generative force and in that way induce locomotion or sustain the beating of the heart. Modeling of muscle tissues active mechanical behavior requires further coupling between mechanical equilibrium and electrical transport. Another unique aspect of soft tissue modeling is their ability to grow, remodel and heal. Modeling these phenomena typically requires coupling field equations from mechanics with biological models. The coupling can be with either kinematic approaches or mixture approaches. The theories covered here are rooted in traditional continuum mechanics models of other soft materials. Yet, as can be seen throughout the chapter, special considerations for soft tissue modeling are needed, which was the central driving force of this chapter. The field of tissue biomechanics has evolved over more than half a century, and now is a good time to step back and note the balance principles, biological rules, and constitutive models that have been developed for soft tissue. We provided both the general theoretical setting but also gave specific examples of constitutive models developed for specific tissues. We anticipate that this chapter will thus be a reference for those with at least a basic continuum mechanics background interested in modeling tissue, to become familiar with the key physical and biological phenomena usually at play in tissue mechanics, and to get a hand on some of the most common models used currently in the field.

Looking toward the future, the last section of this chapter is centered on data-driven constitutive modeling. Machine learning (ML) and artificial intelligence (AI) are reshaping entire engineering fields [212]. Even though for each section we introduced closed form models for each of the physical phenomenon of interest, data-driven tools such as artificial neural networks and Gaussian process regression allow description of constitutive models without explicit analytical forms, giving these approaches much more flexibility and ultimately higher accuracy without a priori assumptions. The time is right for these methods because of the extensive amounts of data gathered in over fifty years of soft tissue characterization research, Nevertheless, obvious concerns are the lack of interpretability and the need to impose physics constraints [192, 194]. These are active areas of investigation that are going to define how, with ever increasing amounts of data, we can build trustworthy ML and AI tools for greater basic science and clinical impact.

Lastly, it should be noted that all soft tissues have received equal attention over the years. Due to the high prevalence of cardiovascular disease, it is not surprising that these tissues have received a significant amount of attention [214]. More recently, focus has shifted to some previously understudied soft

tissues. For instance, reproductive tissue biomechanics has only come to the forefront in the last decade [215, 216]. Brain has also received progressively more attention in recent years. Even though some aspects of brain tissue biomechanics related to traumatic brain injury have been studied for a greater period of time [217], other aspects of brain mechanics, such as mechanical degradation and shrinkage in neuro-psychiatric disease, are only recent areas of investigation [218, 219]. Lastly, the COVID pandemic also highlighted the limited knowledge of pulmonary biomechanics with regards to constitutive modeling of this soft tissue, particularly in the context of infection [220, 221, 222]. We anticipate that these tissues will continue to be at the forefront of soft tissue mechanics research.

References

[1] P. E. Neumann, E. E. Neumann, General histological woes: Definition and classification of tissues, Clinical Anatomy 34 (5) (2021) 794–801.

[2] C. Guillot, T. Lecuit, Mechanics of epithelial tissue homeostasis and morphogenesis, Science 340 (6137) (2013) 1185–1189.

[3] E. Novo, S. Cannito, C. Paternostro, C. Bocca, A. Miglietta, M. Parola, Cellular and molecular mechanisms in liver fibrogenesis, Archives of biochemistry and biophysics 548 (2014) 20–37.

[4] C. V. Falkenberg, E. Jakobsson, A biophysical model for integration of electrical, osmotic, and ph regulation in the human bronchial epithelium, Biophysical journal 98 (8) (2010) 1476–1485.

[5] A. I. Masyuk, R. A. Marinelli, N. F. LaRusso, Water transport by epithelia of the digestive tract, Gastroenterology 122 (2) (2002) 545–562.

[6] S. B. Lemke, C. M. Nelson, Dynamic changes in epithelial cell packing during tissue morphogenesis, Current Biology 31 (18) (2021) R1098–R1110.

[7] H. Elftman, Biomechanics of muscle: with particular application to studies of gait, JBJS 48 (2) (1966) 363–377.

[8] O. Röhrle, J. B. Davidson, A. J. Pullan, A physiologically based, multi-scale model of skeletal muscle structure and function, Frontiers in physiology 3 (2012) 358.

[9] A. E. Ehret, M. Böl, M. Itskov, A continuum constitutive model for the active behaviour of skeletal muscle, Journal of the Mechanics and Physics of Solids 59 (3) (2011) 625–636.

[10] S. Thomopoulos, G. M. Genin, Tendon and ligament biomechanics, Orthopaedic Biomechanics 49 (2012).

[11] X. L. Lu, V. C. Mow, Biomechanics of articular cartilage and determination of material properties, Medicine & Science in Sports & Exercise 40 (2) (2008) 193–199.

[12] S. Park, S. B. Nicoll, R. L. Mauck, G. A. Ateshian, Cartilage mechanical response under dynamic compression at physiological stress levels following collagenase digestion, Annals of Biomedical Engineering 36 (2008) 425–434.

[13] G. Limbert, State-of-the-art constitutive models of skin biomechanics, Computational biophysics of the skin 558 (2014).

[14] W. Zhang, S. Ayoub, J. Liao, M. S. Sacks, A meso-scale layer-specific structural constitutive model of the mitral heart valve leaflets, Acta biomaterialia 32 (2016) 238–255.

[15] W. Buerzle, E. Mazza, On the deformation behavior of human amnion, Journal of biomechanics 46 (11) (2013) 1777–1783.

[16] K. Miller, K. Chinzei, Constitutive modelling of brain tissue: experiment and theory, Journal of biomechanics 30 (11-12) (1997) 1115–1121.

[17] T. Majmudar, S. Balasubramanian, R. Magee, B. Gonik, A. Singh, In-vitro stress relaxation response of neonatal peripheral nerves, Journal of Biomechanics 128 (2021) 110702.

[18] S. Budday, P. Steinmann, E. Kuhl, The role of mechanics during brain development, Journal of the Mechanics and Physics of Solids 72 (2014) 75–92.

[19] Y.-c. Fung, Biomechanics: mechanical properties of living tissues, Springer Science & Business Media, 2013.

[20] W. D. Meador, G. P. Sugerman, H. M. Story, A. W. Seifert, M. R. Bersi, A. B. Tepole, M. K. Rausch, The regional-dependent biaxial behavior of young and aged mouse skin: A detailed histomechanical characterization, residual strain analysis, and constitutive model, Acta biomaterialia 101 (2020) 403–413.

[21] B. N. Safa, M. H. Santare, D. M. Elliott, A reactive inelasticity theoretical framework for modeling viscoelasticity, plastic deformation, and damage in fibrous soft tissue, Journal of Biomechanical Engineering 141 (2) (2019) 021005.

[22] O. Gültekin, G. A. Holzapfel, A brief review on computational modeling of rupture in soft biological tissues, Advances in Computational Plasticity: A Book in Honour of D. Roger J. Owen (2018) 113–144.

[23] R. Spilker, J.-K. Suh, Formulation and evaluation of a finite element model for the biphasic model of hydrated soft tissues, Computers & Structures 35 (4) (1990) 425–439.

[24] G. A. Ateshian, W. Warden, J. Kim, R. Grelsamer, V. C. Mow, Finite deformation biphasic material properties of bovine articular cartilage from confined compression experiments, Journal of biomechanics 30 (11-12) (1997) 1157–1164.

[25] C.-Y. Huang, V. C. Mow, G. A. Ateshian, The role of flow-independent viscoelasticity in the biphasic tensile and compressive responses of articular cartilage, J. Biomech. Eng. 123 (5) (2001) 410–417.

[26] Y. Leng, A. M. Ardekani, H. Gomez, A poro-viscoelastic model for the subcutaneous injection of monoclonal antibodies, Journal of the Mechanics and Physics of Solids 155 (2021) 104537.

[27] Y. Leng, M. de Lucio, H. Gomez, Using poro-elasticity to model the large deformation of tissue during subcutaneous injection, Computer Methods in Applied Mechanics and Engineering 384 (2021) 113919.

[28] A. R. Gillies, R. L. Lieber, Structure and function of the skeletal muscle extracellular matrix, Muscle & nerve 44 (3) (2011) 318–331.

[29] Y. Lanir, Multi-scale structural modeling of soft tissues mechanics and mechanobiology, Journal of Elasticity 129 (1-2) (2017) 7–48.

[30] V. R. Sherman, Y. Tang, S. Zhao, W. Yang, M. A. Meyers, Structural characterization and viscoelastic constitutive modeling of skin, Acta biomaterialia 53 (2017) 460–469.

[31] F. K. Fuss, Anatomy of the cruciate ligaments and their function in extension and flexion of the human knee joint, American Journal of Anatomy 184 (2) (1989) 165–176.

[32] R. de Rooij, E. Kuhl, Constitutive modeling of brain tissue: current perspectives, Applied Mechanics Reviews 68 (1) (2016) 010801.

[33] S. C. Cowin, Tissue growth and remodeling, Annu. Rev. Biomed. Eng. 6 (2004) 77–107.

[34] J. Humphrey, K. Rajagopal, A constrained mixture model for growth and remodeling of soft tissues, Mathematical models and methods in applied sciences 12 (03) (2002) 407–430.

[35] Y. Guo, S. Calve, A. B. Tepole, Multiscale mechanobiology: Coupling models of adhesion kinetics and nonlinear tissue mechanics, Biophysical Journal 121 (4) (2022) 525–539.

[36] E. Kuhl, Growing matter: a review of growth in living systems, Journal of the Mechanical Behavior of Biomedical Materials 29 (2014) 529–543.

[37] S. J. M. Yazdi, J. Baqersad, Mechanical modeling and characterization of human skin: A review, Journal of biomechanics 130 (2022) 110864.

[38] M. F. Leyva-Mendivil, A. Page, N. W. Bressloff, G. Limbert, A mechanistic insight into the mechanical role of the stratum corneum during stretching and compression of the skin, Journal of the Mechanical Behavior of Biomedical Materials 49 (2015) 197–219.

[39] F. Xu, T. Lu, K. Seffen, Biothermomechanics of skin tissues, Journal of the Mechanics and Physics of Solids 56 (5) (2008) 1852–1884.

[40] C. P. Ryan, G. C. Bettelani, S. Ciotti, C. Parise, A. Moscatelli, M. Bianchi, The interaction between motion and texture in the sense of touch, Journal of Neurophysiology 126 (4) (2021) 1375–1390.

[41] O. Moreno-Flores, M. K. Rausch, A. B. Tepole, The role of interface geometry and appendages on the mesoscale mechanics of the skin, Biomechanics and Modeling in Mechanobiology (2023) 1–16.

[42] M. L. Crichton, B. C. Donose, X. Chen, A. P. Raphael, H. Huang, M. A. Kendall, The viscoelastic, hyperelastic and scale dependent behaviour of freshly excised individual skin layers, Biomaterials 32 (20) (2011) 4670–4681.

[43] V. Zarei, S. Zhang, B. A. Winkelstein, V. H. Barocas, Tissue loading and microstructure regulate the deformation of embedded nerve fibres: predictions from single-scale and multiscale simulations, Journal of the Royal Society Interface 14 (135) (2017) 20170326.

[44] R. W. Ogden, Non-linear elastic deformations, Courier Corporation, 1997.

[45] J. Bonet, R. D. Wood, NONLINEAR CONTINUUM MECHANICS FOR FINITE ELEMENT ANALYSIS, Cambridge University Press, United States of America, 1997.

[46] G. A. Holzapfel, Nonlinear solid mechanics: a continuum approach for engineering science (2002).

[47] M. J. Lohr, G. P. Sugerman, S. Kakaletsis, E. Lejeune, M. K. Rausch, An introduction to the ogden model in biomechanics: benefits, implementation tools and limitations, Philosophical Transactions of the Royal Society A 380 (2234) (2022) 20210365.

[48] A. E. Ehret, M. Itskov, A polyconvex hyperelastic model for fiber-reinforced materials in application to soft tissues, Journal of Materials Science 42 (2007) 8853–8863.

[49] R. W. Ogden, Large deformation isotropic elasticity – on the correlation of theory and experiment for incompressible rubberlike solids (1972) 20.

[50] A. Anssari-Benam, M. Destrade, G. Saccomandi, Modelling brain tissue elasticity with the ogden model and an alternative family of constitutive models, Philosophical Transactions of the Royal Society A 380 (2234) (2022) 20210325.

[51] K. Comley, N. Fleck, The mechanical response of porcine adipose tissue, ASME Journal of Biomechanical Engineering (2009) 1–30.

[52] M. K. Rausch, G. P. Sugerman, S. Kakaletsis, B. Dortdivanlioglu, Hyper-viscoelastic damage modeling of whole blood clot under large deformation, Biomechanics and Modeling in Mechanobiology 20 (5) (2021) 1645–1657.

[53] P. G. Ciarlet, Mathematical elasticity: Three-dimensional elasticity, SIAM, 2021.

[54] R. Fan, M. S. Sacks, Simulation of planar soft tissues using a structural constitutive model: finite element implementation and validation, Journal of biomechanics 47 (9) (2014) 2043–2054.

[55] T. C. Gasser, R. W. Ogden, G. A. Holzapfel, Hyperelastic modelling of arterial layers with distributed collagen fibre orientations, Journal of The Royal Society Interface 3 (6) (2006) 15–35. doi:10.1098/rsif.2005.0073.

[56] G. A. Holzapfel, et al., Biomechanics of soft tissue, The handbook of materials behavior models 3 (1) (2001) 1049–1063.

[57] G. A. Holzapfel, R. W. Ogden, S. Sherifova, On fibre dispersion modelling of soft biological tissues: a review, Proceedings of the Royal Society A 475 (2224) (2019) 20180736.

[58] K. May-Newman, F. Yin, A constitutive law for mitral valve tissue (1998).

[59] A. Wahlsten, M. Pensalfini, A. Stracuzzi, G. Restivo, R. Hopf, E. Mazza, On the compressibility and poroelasticity of human and murine skin, Biomechanics and modeling in mechanobiology 18 (2019) 1079–1093.

[60] D. M. Pierce, T. Ricken, G. A. Holzapfel, A hyperelastic biphasic fibre-reinforced model of articular cartilage considering distributed collagen fibre orientations: continuum basis, computational aspects and applications, Computer methods in biomechanics and biomedical engineering 16 (12) (2013) 1344–1361.

[61] E. Pena, B. Calvo, M. Martínez, M. Doblaré, An anisotropic visco-hyperelastic model for ligaments at finite strains. formulation and computational aspects, International Journal of Solids and Structures 44 (3-4) (2007) 760–778.

[62] A. N. Annaidh, K. Bruyère, M. Destrade, M. D. Gilchrist, M. Otténio, Characterization of the anisotropic mechanical properties of excised human skin, Journal of the mechanical behavior of biomedical materials 5 (1) (2012) 139–148.

[63] V. D. Sree, J. D. Toaquiza-Tubon, J. Payne, L. Solorio, A. B. Tepole, Damage and fracture mechanics of porcine subcutaneous tissue under tensile loading, Annals of Biomedical Engineering 51 (9) (2023) 2056–2069.

[64] C. M. Luetkemeyer, U. Scheven, J. B. Estrada, E. M. Arruda, Constitutive modeling of the anterior cruciate ligament bundles and patellar tendon with full-field methods, Journal of the Mechanics and Physics of Solids 156 (2021) 104577.

[65] G. Sommer, A. J. Schriefl, M. Andrä, M. Sacherer, C. Viertler, H. Wolinski, G. A. Holzapfel, Biomechanical properties and microstructure of human ventricular myocardium, Acta biomaterialia 24 (2015) 172–192.

[66] S. Kakaletsis, W. D. Meador, M. Mathur, G. P. Sugerman, T. Jazwiec, M. Malinowski, E. Lejeune, T. A. Timek, M. K. Rausch, Right ventricular myocardial mechanics: Multi-modal deformation, microstructure, modeling, and comparison to the left ventricle, Acta biomaterialia 123 (2021) 154–166.

[67] J. J. Sarver, P. S. Robinson, D. M. Elliott, Methods for quasi-linear viscoelastic modeling of soft tissue: application to incremental stress-relaxation experiments, J. Biomech. Eng. 125 (5) (2003) 754–758.

[68] R. Cohen, C. Hooley, N. McCrum, Viscoelastic creep of collagenous tissue, Journal of biomechanics 9 (4) (1976) 175–184.

[69] S. Govindjee, S. Reese, A presentation and comparison of two large deformation viscoelasticity models (1997).

[70] S. Reese, S. Govindjee, A theory of finite viscoelasticity and numerical aspects, International journal of solids and structures 35 (26-27) (1998) 3455–3482.

[71] K. Upadhyay, G. Subhash, D. Spearot, Visco-hyperelastic constitutive modeling of strain rate sensitive soft materials, Journal of the Mechanics and Physics of Solids 135 (2020) 103777.

[72] A. Nekouzadeh, K. M. Pryse, E. L. Elson, G. M. Genin, A simplified approach to quasi-linear viscoelastic modeling, Journal of biomechanics 40 (14) (2007) 3070–3078.

[73] R. S. Lakes, Viscoelastic materials, Cambridge university press, 2009.

[74] G. Del Piero, L. Deseri, On the concepts of state and free energy in linear viscoelasticity, Archive for Rational Mechanics and Analysis 138 (1) (1997) 1.

[75] M. Enelund, P. Olsson, Damping described by fading memory—analysis and application to fractional derivative models, International Journal of Solids and Structures 36 (7) (1999) 939–970.

[76] M. Puso, J. Weiss, Finite element implementation of anisotropic quasi-linear viscoelasticity using a discrete spectrum approximation (1998).

[77] S. A. Maas, B. J. Ellis, G. A. Ateshian, J. A. Weiss, Febio: finite elements for biomechanics, Journal of biomechanical engineering 134 (1) (2012).

[78] G. A. Holzapfel, T. C. Gasser, M. Stadler, A structural model for the viscoelastic behavior of arterial walls: continuum formulation and finite element analysis, European Journal of Mechanics-A/Solids 21 (3) (2002) 441–463.

[79] J. L. Calvo-Gallego, J. Domínguez, T. G. Cía, G. G. Ciriza, J. Martínez-Reina, Comparison of different constitutive models to characterize the viscoelastic properties of human abdominal adipose tissue. a pilot study, Journal of the mechanical behavior of biomedical materials 80 (2018) 293–302.

[80] A. Bonfanti, J. L. Kaplan, G. Charras, A. Kabla, Fractional viscoelastic models for power-law materials, Soft Matter 16 (26) (2020) 6002–6020.

[81] Y. Kobayashi, M. Tsukune, T. Miyashita, M. G. Fujie, Simple empirical model for identifying rheological properties of soft biological tissues, Physical Review E 95 (2) (2017) 022418.

[82] I. Podlubny, Fractional differential equations: an introduction to fractional derivatives, fractional differential equations, to methods of their solution and some of their applications, Elsevier, 1998.

[83] W. Zhang, J. Jilberto, G. Sommer, M. S. Sacks, G. A. Holzapfel, D. A. Nordsletten, Simulating hyperelasticity and fractional viscoelasticity in the human heart, Computer Methods in Applied Mechanics and Engineering 411 (2023) 116048.

[84] W. Zhang, A. Capilnasiu, G. Sommer, G. A. Holzapfel, D. A. Nordsletten, An efficient and accurate method for modeling nonlinear fractional viscoelastic biomaterials, Computer methods in applied mechanics and engineering 362 (2020) 112834.

[85] B. Moran, M. Ortiz, C. Shih, Formulation of implicit finite element methods for multiplicative finite deformation plasticity, International Journal for Numerical Methods in Engineering 29 (3) (1990) 483–514.

[86] S. Nemat-Nasser, On finite deformation elasto-plasticity, International Journal of Solids and Structures 18 (10) (1982) 857–872.

[87] T. Nguyen, R. Jones, B. Boyce, A nonlinear anisotropic viscoelastic model for the tensile behavior of the corneal stroma (2008).

[88] J. Vassoler, L. Reips, E. Fancello, A variational framework for fiber-reinforced viscoelastic soft tissues, International Journal for Numerical Methods in Engineering 89 (13) (2012) 1691–1706.

[89] V. Taç, M. K. Rausch, F. S. Costabal, A. B. Tepole, Data-driven anisotropic finite viscoelasticity using neural ordinary differential equations, Computer Methods in Applied Mechanics and Engineering 411 (2023) 116046.

[90] T. Nguyen, R. Jones, B. Boyce, Modeling the anisotropic finite-deformation viscoelastic behavior of soft fiber-reinforced composites, International Journal of Solids and Structures 44 (25-26) (2007) 8366–8389. doi:10.1016/j.ijsolstr.2007.06.020.

[91] J. M. Jimenez, T. Tuttle, Y. Guo, D. Miles, A. Buganza-Tepole, S. Calve, Multiscale mechanical characterization and computational modeling of fibrin gels, Acta biomaterialia 162 (2023) 292–303.

[92] M. Ottenio, D. Tran, A. N. Annaidh, M. D. Gilchrist, K. Bruyère, Strain rate and anisotropy effects on the tensile failure characteristics of human skin, Journal of the mechanical behavior of biomedical materials 41 (2015) 241–250.

[93] M. R. Islam, J. Virag, M. L. Oyen, Micromechanical poroelastic and viscoelastic properties of ex-vivo soft tissues, Journal of Biomechanics 113 (2020) 110090.

[94] W. Yao, K. Yoshida, M. Fernandez, J. Vink, R. J. Wapner, C. V. Ananth, M. L. Oyen, K. M. Myers, Measuring the compressive viscoelastic mechanical properties of human cervical tissue using indentation, Journal of the mechanical behavior of biomedical materials 34 (2014) 18–26.

[95] A. E. Ehret, M. Hollenstein, E. Mazza, M. Itskov, Porcine dermis in uniaxial cyclic loading: sample preparation, experimental results and modeling, Journal of Mechanics of Materials and Structures 6 (7) (2011) 1125–1135.

[96] S. Murakami, Continuum damage mechanics: a continuum mechanics approach to the analysis of damage and fracture, Vol. 185, Springer Science & Business Media, 2012.

[97] J. C. Simo, J. Ju, Strain-and stress-based continuum damage models—i. formulation, International journal of solids and structures 23 (7) (1987) 821–840.

[98] C. Hesch, A. Gil, R. Ortigosa, M. Dittmann, C. Bilgen, P. Betsch, M. Franke, A. Janz, K. Weinberg, A framework for polyconvex large strain phase-field methods to fracture, Computer Methods in Applied Mechanics and Engineering 317 (2017) 649–683.

[99] C. Miehe, F. Aldakheel, A. Raina, Phase field modeling of ductile fracture at finite strains: A variational gradient-extended plasticity-damage theory, International Journal of Plasticity 84 (2016) 1–32.

[100] R. W. Ogden, D. G. Roxburgh, A pseudo–elastic model for the mullins effect in filled rubber, Proceedings of the Royal Society of London. Series A: Mathematical, Physical and Engineering Sciences 455 (1988) (1999) 2861–2877.

[101] L. Mullins, Effect of stretching on the properties of rubber, Rubber chemistry and technology 21 (2) (1948) 281–300.

[102] L. Zhan, S. Wang, S. Qu, P. Steinmann, R. Xiao, A general continuum damage model for soft composites, Journal of the Mechanics and Physics of Solids 175 (2023) 105290.

[103] S. Govindjee, J. Simo, A micro-mechanically based continuum damage model for carbon black-filled rubbers incorporating mullins' effect, Journal of the Mechanics and Physics of Solids 39 (1) (1991) 87–112.

[104] S. Göktepe, C. Miehe, A micro–macro approach to rubber-like materials. part iii: The micro-sphere model of anisotropic mullins-type damage, Journal of the Mechanics and Physics of Solids 53 (10) (2005) 2259–2283.

[105] W. Li, Damage models for soft tissues: a survey, Journal of Medical and Biological Engineering 36 (2016) 285–307.

[106] B. Calvo, E. Peña, M. Martinez, M. Doblaré, An uncoupled directional damage model for fibred biological soft tissues. formulation and computational aspects, International journal for numerical methods in engineering 69 (10) (2007) 2036–2057.

[107] D. Balzani, T. Schmidt, Comparative analysis of damage functions for soft tissues: Properties at damage initialization, Mathematics and mechanics of solids 20 (4) (2015) 480–492.

[108] E. Peña, Damage functions of the internal variables for soft biological fibred tissues, Mechanics Research Communications 38 (8) (2011) 610–615.

[109] C. Martin, W. Sun, Modeling of long-term fatigue damage of soft tissue with stress softening and permanent set effects, Biomechanics and modeling in mechanobiology 12 (2013) 645–655.

[110] J. Carmeliet, D. Derome, M. Dressler, R. A. Guyer, Nonlinear poroelastic model for unsaturated porous solids, Journal of Applied Mechanics 80 (2) (2013) 020909.

[111] Y. Hu, Z. Suo, Viscoelasticity and poroelasticity in elastomeric gels, Acta Mechanica Solida Sinica 25 (5) (2012) 441–458.

[112] V. C. Mow, S. Kuei, W. M. Lai, C. G. Armstrong, Biphasic creep and stress relaxation of articular cartilage in compression: theory and experiments (1980).

[113] V. C. Mow, M. H. Holmes, W. M. Lai, Fluid transport and mechanical properties of articular cartilage: a review, Journal of biomechanics 17 (5) (1984) 377–394.

[114] M. Holmes, V. C. Mow, The nonlinear characteristics of soft gels and hydrated connective tissues in ultrafiltration, Journal of biomechanics 23 (11) (1990) 1145–1156.

[115] G. A. Ateshian, J. A. Weiss, Anisotropic hydraulic permeability under finite deformation (2010).

[116] E. Rahimi, S. Aramideh, D. Han, H. Gomez, A. M. Ardekani, Transport and lymphatic uptake of monoclonal antibodies after subcutaneous injection, Microvascular Research 139 (2022) 104228.

[117] M. Thomsen, A. Hernandez-Garcia, J. Mathiesen, M. Poulsen, D. N. Sørensen, L. Tarnow, R. Feidenhans'l, Model study of the pressure build-up during subcutaneous injection, PloS one 9 (8) (2014) e104054.

[118] M. Hosseini-Farid, M. Ramzanpour, J. McLean, M. Ziejewski, G. Karami, A poro-hyper-viscoelastic rate-dependent constitutive modeling for the analysis of brain tissues, Journal of the Mechanical Behavior of Biomedical Materials 102 (2020) 103475.

[119] L. Su, M. Wang, J. Yin, F. Ti, J. Yang, C. Ma, S. Liu, T. J. Lu, Distinguishing poroelasticity and viscoelasticity of brain tissue with time scale, Acta Biomaterialia 155 (2023) 423–435.

[120] F. Concha, D. E. Hurtado, Upscaling the poroelastic behavior of the lung parenchyma: A finite-deformation micromechanical model, Journal of the Mechanics and Physics of Solids 145 (2020) 104147.

[121] L. Berger, R. Bordas, K. Burrowes, V. Grau, S. Tavener, D. Kay, A poroelastic model coupled to a fluid network with applications in lung modelling, International journal for numerical methods in biomedical engineering 32 (1) (2016).

[122] M.-J. Weir Weiss, P. Shrestha, R. Basak, B. Stoeber, Poroelastic behavior of skin tissue in response to pressure driven flow, Physics of Fluids 35 (8) (2023).

[123] S. Kalyanam, K. S. Toohey, M. F. Insana, Modeling biphasic hydrogels under spherical indentation: Application to soft tissues, Mechanics of Materials 161 (2021) 103987.

[124] A. Bach, J. Stern-Straeter, J. Beier, H. Bannasch, G. Stark, Engineering of muscle tissue, Clinics in plastic surgery 30 (4) (2003) 589–599.

[125] S. Loerakker, C. Obbink-Huizer, F. P. Baaijens, A physically motivated constitutive model for cell-mediated compaction and collagen remodeling in soft tissues, Biomechanics and modeling in mechanobiology 13 (2014) 985–1001.

[126] G. Odegard, T. Haut Donahue, D. Morrow, K. R. Kaufman, Constitutive modeling of skeletal muscle tissue with an explicit strain-energy function (2008).

[127] D. H. Cortes, D. M. Elliott, Modeling of collagenous tissues using distributed fiber orientations, in: Structure-based mechanics of tissues and organs, Springer, 2016, pp. 15–39.

[128] F. Regazzoni, L. Dedè, A. Quarteroni, Active contraction of cardiac cells: a reduced model for sarcomere dynamics with cooperative interactions, Biomechanics and modeling in mechanobiology 17 (6) (2018) 1663–1686.

[129] J. Wong, S. Göktepe, E. Kuhl, Computational modeling of electrochemical coupling: a novel finite element approach towards ionic models for cardiac electrophysiology, Computer methods in applied mechanics and engineering 200 (45-46) (2011) 3139–3158.

[130] T. Tan, R. De Vita, A structural constitutive model for smooth muscle contraction in biological tissues, International Journal of Non-Linear Mechanics 75 (2015) 46–53.

[131] A. Schmitz, M. Böl, On a phenomenological model for active smooth muscle contraction, Journal of biomechanics 44 (11) (2011) 2090–2095.

[132] L. Bursztyn, O. Eytan, A. J. Jaffa, D. Elad, Mathematical model of excitation-contraction in a uterine smooth muscle cell, American Journal of Physiology-Cell Physiology 292 (5) (2007) C1816–C1829.

[133] R. D. Kamm, Airway wall mechanics, Annual review of biomedical engineering 1 (1) (1999) 47–72.

[134] S. Göktepe, E. Kuhl, Electromechanics of the heart: a unified approach to the strongly coupled excitation–contraction problem, Computational Mechanics 45 (2010) 227–243.

[135] M. P. Nash, A. V. Panfilov, Electromechanical model of excitable tissue to study reentrant cardiac arrhythmias, Progress in biophysics and molecular biology 85 (2-3) (2004) 501–522.

[136] A. L. Hodgkin, A. F. Huxley, A quantitative description of membrane current and its application to conduction and excitation in nerve, The Journal of physiology 117 (4) (1952) 500.

[137] S. Göktepe, E. Kuhl, Computational modeling of cardiac electrophysiology: a novel finite element approach, International journal for numerical methods in engineering 79 (2) (2009) 156–178.

[138] A. Quarteroni, T. Lassila, S. Rossi, R. Ruiz-Baier, Integrated heart—coupling multiscale and multiphysics models for the simulation of the cardiac function, Computer Methods in Applied Mechanics and Engineering 314 (2017) 345–407.

[139] N. A. Trayanova, J. J. Rice, Cardiac electromechanical models: from cell to organ, Frontiers in physiology 2 (2011) 43.

[140] R. Clayton, A. Panfilov, A guide to modelling cardiac electrical activity in anatomically detailed ventricles, Progress in biophysics and molecular biology 96 (1-3) (2008) 19–43.

[141] K. S. Kolahi, M. R. Mofrad, Mechanotransduction: a major regulator of homeostasis and development, Wiley Interdisciplinary Reviews: Systems Biology and Medicine 2 (6) (2010) 625–639.

[142] Y. Guo, M. R. Mofrad, A. B. Tepole, On modeling the multiscale mechanobiology of soft tissues: Challenges and progress, Biophysics Reviews 3 (3) (2022).

[143] E. K. Rodriguez, A. Hoger, A. D. McCulloch, Stress-dependent finite growth in soft elastic tissues, Journal of biomechanics 27 (4) (1994) 455–467.

[144] J. Li, M. Kothari, S. Chockalingam, T. Henzel, Q. Zhang, X. Li, J. Yan, T. Cohen, Nonlinear inclusion theory with application to the growth and morphogenesis of a confined body, Journal of the Mechanics and Physics of Solids 159 (2022) 104709.

[145] A. Menzel, E. Kuhl, Frontiers in growth and remodeling, Mechanics research communications 42 (2012) 1–14.

[146] M. A. Holland, K. E. Miller, E. Kuhl, Emerging brain morphologies from axonal elongation, Annals of biomedical engineering 43 (2015) 1640–1653.

[147] M. A. Holland, T. Kosmata, A. Goriely, E. Kuhl, On the mechanics of thin films and growing surfaces, Mathematics and Mechanics of Solids 18 (6) (2013) 561–575.

[148] S. Göktepe, O. J. Abilez, E. Kuhl, A generic approach towards finite growth with examples of athlete's heart, cardiac dilation, and cardiac wall thickening, Journal of the Mechanics and Physics of Solids 58 (10) (2010) 1661–1680.

[149] M. Rausch, A. Dam, S. Göktepe, O. Abilez, E. Kuhl, Computational modeling of growth: systemic and pulmonary hypertension in the heart, Biomechanics and modeling in mechanobiology 10 (2011) 799–811.

[150] T. Han, T. Lee, J. Ledwon, E. Vaca, S. Turin, A. Kearney, A. K. Gosain, A. B. Tepole, Bayesian calibration of a computational model of tissue expansion based on a porcine animal model, Acta biomaterialia 137 (2022) 136–146.

[151] T. Lee, E. E. Vaca, J. K. Ledwon, H. Bae, J. M. Topczewska, S. Y. Turin, E. Kuhl, A. K. Gosain, A. B. Tepole, Improving tissue expansion protocols through computational modeling, Journal of the mechanical behavior of biomedical materials 82 (2018) 224–234.

[152] J. LoGiudice, A. K. Gosain, Pediatric tissue expansion: indications and complications, Plastic and Aesthetic Nursing 24 (1) (2004) 20–26.

[153] A. K. Gosain, C. G. Zochowski, W. Cortes, Refinements of tissue expansion for pediatric forehead reconstruction: a 13-year experience, Plastic and reconstructive surgery 124 (5) (2009) 1559–1570.

[154] T. Han, K. S. Ahmed, A. K. Gosain, A. B. Tepole, T. Lee, Multi-fidelity gaussian process surrogate modeling of pediatric tissue expansion, Journal of Biomechanical Engineering 144 (12) (2022) 121005.

[155] N. Bertozzi, M. Pesce, P. Santi, E. Raposio, Tissue expansion for breast reconstruction: Methods and techniques, Annals of medicine and surgery 21 (2017) 34–44.

[156] G. A. Ateshian, On the theory of reactive mixtures for modeling biological growth, Biomechanics and modeling in mechanobiology 6 (2007) 423–445.

[157] C. Cyron, R. Aydin, J. Humphrey, A homogenized constrained mixture (and mechanical analog) model for growth and remodeling of soft tissue, Biomechanics and modeling in mechanobiology 15 (6) (2016) 1389–1403.

[158] M. K. Rausch, J. D. Humphrey, A computational model of the biochemomechanics of an evolving occlusive thrombus, Journal of Elasticity 129 (1) (2017) 125–144.

[159] C. Truesdell, R. Toupin, The classical field theories, in: Principles of classical mechanics and field theory/Prinzipien der Klassischen Mechanik und Feldtheorie, Springer, 1960, pp. 226–858.

[160] A. Valentin, J. Humphrey, Evaluation of fundamental hypotheses underlying constrained mixture models of arterial growth and remodelling, Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 367 (1902) (2009) 3585–3606.

[161] M. Latorre, J. D. Humphrey, A mechanobiologically equilibrated constrained mixture model for growth and remodeling of soft tissues, ZAMM-Journal of Applied Mathematics and Mechanics/Zeitschrift für Angewandte Mathematik und Mechanik 98 (12) (2018) 2048–2071.

[162] A. Valentin, J. D. Humphrey, G. A. Holzapfel, A finite element-based constrained mixture implementation for arterial growth, remodeling, and adaptation: Theory and numerical verification, International journal for numerical methods in biomedical engineering 29 (8) (2013) 822–849.

[163] M. Latorre, J. D. Humphrey, Fast, rate-independent, finite element implementation of a 3d constrained mixture model of soft tissue growth and remodeling, Computer methods in applied mechanics and engineering 368 (2020) 113156.

[164] J. F. Eichinger, M. J. Grill, I. D. Kermani, R. C. Aydin, W. A. Wall, J. D. Humphrey, C. J. Cyron, A computational framework for modeling cell–matrix interactions in soft biological tissues, Biomechanics and modeling in mechanobiology 20 (5) (2021) 1851–1870.

[165] P. Moreo, J. M. García-Aznar, M. Doblaré, Modeling mechanosensing and its effect on the migration and proliferation of adherent cells, Acta biomaterialia 4 (3) (2008) 613–621.

[166] A. Raina, C. Linder, A homogenization approach for nonwoven materials based on fiber undulations and reorientation, Journal of the Mechanics and Physics of Solids 65 (2014) 12–34.

[167] A. Menzel, A fibre reorientation model for orthotropic multiplicative growth: configurational driving stresses, kinematics-based reorientation, and algorithmic aspects, Biomechanics and modeling in mechanobiology 6 (2007) 303–320.

[168] A. B. Tepole, Computational systems mechanobiology of wound healing, Computer methods in applied mechanics and engineering 314 (2017) 46–70.

[169] D. O. Sohutskay, A. B. Tepole, S. L. Voytik-Harbin, Mechanobiological wound model for improved design and evaluation of collagen dermal replacement scaffolds, Acta biomaterialia 135 (2021) 368–382.

[170] S. Loerakker, T. Ristori, F. P. Baaijens, A computational analysis of cell-mediated compaction and collagen remodeling in tissue-engineered heart valves, Journal of the mechanical behavior of biomedical materials 58 (2016) 173–187.

[171] C. Obbink-Huizer, C. W. Oomens, S. Loerakker, J. Foolen, C. V. Bouten, F. P. Baaijens, Computational model predicts cell orientation in response to a range of mechanical stimuli, Biomechanics and modeling in mechanobiology 13 (2014) 227–236.

[172] M. Pensalfini, A. B. Tepole, Mechano-biological and bio-mechanical pathways in cutaneous wound healing, PLoS computational biology 19 (3) (2023) e1010902.

[173] A. Buganza Tepole, E. Kuhl, Computational modeling of chemo-bio-mechanical coupling: a systems-biology approach toward wound healing, Computer methods in biomechanics and biomedical engineering 19 (1) (2016) 13–30.

[174] S. H. Kwon, J. Padmanabhan, G. C. Gurtner, Mechanobiology of skin diseases and wound healing, in: Mechanobiology in Health and Disease, Elsevier, 2018, pp. 415–448.

[175] F. H. Silver, L. M. Siperko, G. P. Seehra, Mechanobiology of force transduction in dermal tissue, Skin Research and Technology 9 (1) (2003) 3–23.

[176] S. Werner, T. Krieg, H. Smola, Keratinocyte–fibroblast interactions in wound healing, Journal of investigative dermatology 127 (5) (2007) 998–1008.

[177] S. Y. Kim, M. G. Nair, Macrophages in wound healing: activation and plasticity, Immunology and cell biology 97 (3) (2019) 258–267.

[178] T. J. Koh, L. A. DiPietro, Inflammation and wound healing: the role of the macrophage, Expert reviews in molecular medicine 13 (2011) e23.

[179] J. A. Flegg, S. N. Menon, P. K. Maini, D. S. McElwain, On the mathematical modeling of wound healing angiogenesis in skin as a reaction-transport process, Frontiers in physiology 6 (2015) 262.

[180] A. Buganza Tepole, E. Kuhl, Systems-based approaches toward wound healing, Pediatric research 73 (2) (2013) 553–563.

[181] S. a. Guo, L. A. DiPietro, Factors affecting wound healing, Journal of dental research 89 (3) (2010) 219–229.

[182] J. D. Humphrey, S. L. O'Rourke, An Introduction to Biomechanics, Springer New York, New York, NY, 2015. doi:10.1007/978-1-4939-2623-7.

[183] K. Hornik, M. Stinchcombe, H. White, Multilayer feedforward networks are universal approximators, Neural Networks 2 (5) (1989) 359–366. doi:10.1016/0893-6080(89)90020-8.

[184] H. Dal, K. Açıkgöz, Y. Badienia, On the Performance of Isotropic Hyperelastic Constitutive Models for Rubber-Like Materials: A State of the Art Review, Applied Mechanics Reviews 73 (2) (2021) 020802. doi:10.1115/1.4050978.

[185] G. Limbert (Ed.), Skin Biophysics: From Experimental Characterisation to Advanced Modelling, Vol. 22 of Studies in Mechanobiology, Tissue Engineering and Biomaterials, Springer International Publishing, Cham, 2019. doi:10.1007/978-3-030-13279-8.

[186] M. Liu, L. Liang, W. Sun, A generic physics-informed neural network-based constitutive model for soft biological tissues, Computer Methods in Applied Mechanics and Engineering 372 (2020) 113402. doi:10.1016/j.cma.2020.113402.

[187] V. Tac, V. D. Sree, M. K. Rausch, A. B. Tepole, Data-driven modeling of the mechanical behavior of anisotropic soft biological tissue, Engineering with Computers 38 (5) (2022) 4167–4182. doi:10.1007/s00366-022-01733-3.

[188] J. M. Ball, Convexity conditions and existence theorems in nonlinear elasticity, Archive for Rational Mechanics and Analysis 63 (4) (1976) 337–403. doi:10.1007/BF00279992.

[189] D. Balzani, P. Neff, J. Schröder, G. Holzapfel, A polyconvex framework for soft biological tissues. Adjustment to experimental data, International Journal of Solids and Structures 43 (20) (2006) 6052–6070. doi:10.1016/j.ijsolstr.2005.07.048.

[190] V. Tac, F. S. Costabal, A. B. Tepole, Data-driven tissue mechanics with polyconvex neural ordinary differential equations, Computer Methods in Applied Mechanics and Engineering 398 (2022) 18. doi:10.1016/j.cma.2022.115248.

[191] D. K. Klein, F. J. Roth, I. Valizadeh, O. Weeger, Parametrised polyconvex hyperelasticity with physics-augmented neural networks (Jul. 2023). arXiv:2307.03463.

[192] K. Linka, E. Kuhl, A new family of Constitutive Artificial Neural Networks towards automated model discovery (Oct. 2022). arXiv:2210.02202.

[193] M. Flaschel, S. Kumar, L. De Lorenzis, Unsupervised discovery of interpretable hyperelastic constitutive laws, Computer Methods in Applied Mechanics and Engineering 381 (2021) 113852. doi:10.1016/j.cma.2021.113852.

[194] V. Taç, K. Linka, F. Sahli-Costabal, E. Kuhl, A. B. Tepole, Benchmarking physics-informed frameworks for data-driven hyperelasticity, Computational Mechanics (Jun. 2023). doi:10.1007/s00466-023-02355-2.

[195] M. Rosenkranz, K. A. Kalina, J. Brummund, M. Kästner, A comparative study on different neural network architectures to model inelasticity, International Journal for Numerical Methods in Engineering (2023) nme.7319doi:10.1002/nme.7319.

[196] H. Salahshoor, M. Ortiz, Model-Free Data-Driven Viscoelasticity in the Frequency Domain (May 2022). arXiv:2205.06674.

[197] K. Xu, A. M. Tartakovsky, J. Burghardt, E. Darve, Learning viscoelasticity models from indirect data using deep neural networks, Computer Methods in Applied Mechanics and Engineering 387 (2021) 114124. doi:10.1016/j.cma.2021.114124.

[198] F. As'ad, C. Farhat, A mechanics-informed deep learning framework for data-driven nonlinear viscoelasticity, Computer Methods in Applied Mechanics and Engineering 417 (2023) 116463. doi:10.1016/j.cma.2023.116463.

[199] M. Rosenkranz, K. A. Kalina, J. Brummund, W. Sun, M. Kästner, Viscoelasticty with physics-augmented neural networks: Model formulation and training methods without prescribed internal variables (Jan. 2024). arXiv:2401.14270.

[200] L. M. Wang, K. Linka, E. Kuhl, Automated model discovery for muscle using constitutive recurrent neural networks, Journal of the Mechanical Behavior of Biomedical Materials 145 (2023) 106021. doi:10.1016/j.jmbbm.2023.106021.

[201] E. Marino, M. Flaschel, S. Kumar, L. De Lorenzis, Automated identification of linear viscoelastic constitutive laws with EUCLID, Mechanics of Materials 181 (2023) 104643. doi:10.1016/j.mechmat.2023.104643.

[202] M. Yin, E. Ban, B. V. Rego, E. Zhang, C. Cavinato, J. D. Humphrey, G. Em Karniadakis, Simulating progressive intramural damage leading to aortic dissection using DeepONet: An operator–regression neural network, Journal of The Royal Society Interface 19 (187) (2022) 20210670. doi:10.1098/rsif.2021.0670.

[203] M. Miñano, F. J. Montáns, WYPiWYG Damage Mechanics for Soft Materials: A Data-Driven Approach, Archives of Computational Methods in Engineering 25 (1) (2018) 165–193. doi:10.1007/s11831-017-9233-4.

[204] S. Saha, Z. Gan, L. Cheng, J. Gao, O. L. Kafka, X. Xie, H. Li, M. Tajdari, H. A. Kim, W. K. Liu, Hierarchical Deep Learning Neural Network (HiDeNN): An artificial intelligence (AI) framework for computational science and engineering, Computer Methods in Applied Mechanics and Engineering 373 (2021) 113452. doi:10.1016/j.cma.2020.113452.

[205] F. Feyel, J.-L. Chaboche, FE2 multiscale approach for modelling the elastoviscoplastic behaviour of long fibre SiC/Ti composite materials, Computer Methods in Applied Mechanics and Engineering 183 (3) (2000) 309–330. doi:10.1016/S0045-7825(99)00224-8.

[206] D. Reimann, K. Nidadavolu, H. Ul Hassan, N. Vajragupta, T. Glasmachers, P. Junker, A. Hartmaier, Modeling Macroscopic Material Behavior With Machine Learning Algorithms Trained by Micromechanical Simulations, Frontiers in Materials 6 (2019) 181. doi:10.3389/fmats.2019.00181.

[207] G. C. Y. Peng, M. Alber, A. Buganza Tepole, W. R. Cannon, S. De, S. Dura-Bernal, K. Garikipati, G. Karniadakis, W. W. Lytton, P. Perdikaris, L. Petzold, E. Kuhl, Multiscale Modeling Meets Machine Learning: What Can We Learn?, Archives of Computational Methods in Engineering 28 (3) (2021) 1017–1037. doi:10.1007/s11831-020-09405-5.

[208] Y. Leng, V. Tac, S. Calve, A. B. Tepole, Predicting the mechanical properties of biopolymer gels using neural networks trained on discrete fiber network data, Computer Methods in Applied Mechanics and Engineering 387 (2021) 114160. doi:10.1016/j.cma.2021.114160.

[209] M. Fernández, M. Jamshidian, T. Böhlke, K. Kersting, O. Weeger, Anisotropic hyperelastic constitutive models for finite deformations combining material theory and data-driven approaches with application to cubic lattice metamaterials, Computational Mechanics 67 (2) (2021) 653–677. doi:10.1007/s00466-020-01954-7.

[210] C. Settgast, G. Hütter, M. Kuna, M. Abendroth, A hybrid approach to simulate the homogenized irreversible elastic–plastic deformations and damage of foams by neural networks, International Journal of Plasticity 126 (2020) 102624. doi:10.1016/j.ijplas.2019.11.003.

[211] K. A. Kalina, L. Linden, J. Brummund, M. Kästner, FE^{ANN}: An efficient data-driven multiscale approach based on physics-constrained neural networks and automated data mining, Computational Mechanics 71 (5) (2023) 827–851. doi:10.1007/s00466-022-02260-0.

[212] M. Alber, A. Buganza Tepole, W. R. Cannon, S. De, S. Dura-Bernal, K. Garikipati, G. Karniadakis, W. W. Lytton, P. Perdikaris, L. Petzold, et al., Integrating machine learning and multiscale modeling—perspectives, challenges, and opportunities in the biological, biomedical, and behavioral sciences, NPJ digital medicine 2 (1) (2019) 115.

[213] V. Tac, M. K. Rausch, I. Bilionis, F. S. Costabal, A. B. Tepole, Generative hyperelasticity with physics-informed probabilistic diffusion fields, arXiv preprint arXiv:2310.03745 (2023).

[214] C. A. Taylor, C. Figueroa, Patient-specific modeling of cardiovascular mechanics, Annual review of biomedical engineering 11 (2009) 109–134.

[215] K. M. Myers, D. Elad, Biomechanics of the human uterus, Wiley Interdisciplinary Reviews: Systems Biology and Medicine 9 (5) (2017) e1388.

[216] A. Baah-Dwomoh, J. McGuire, T. Tan, R. De Vita, Mechanical properties of female reproductive organs and supporting connective tissues: a review of the current state of knowledge, Applied Mechanics Reviews 68 (6) (2016) 060801.

[217] T. El Sayed, A. Mota, F. Fraternali, M. Ortiz, Biomechanics of traumatic brain injury, Computer Methods in Applied Mechanics and Engineering 197 (51-52) (2008) 4692–4701.

[218] Y. Blinkouskaya, A. Caçoilo, T. Gollamudi, S. Jalalian, J. Weickenmeier, Brain aging mechanisms with mechanical manifestations, Mechanisms of ageing and development 200 (2021) 111575.

[219] A. Schäfer, J. Weickenmeier, E. Kuhl, The interplay of biochemical and biomechanical degeneration in alzheimer's disease, Computer methods in applied mechanics and engineering 352 (2019) 369–388.

[220] M. Eskandari, T. M. Nordgren, G. D. O'Connell, Mechanics of pulmonary airways: linking structure to function through constitutive modeling, biochemistry, and histology, Acta biomaterialia 97 (2019) 513–523.

[221] B. Suki, J. Bates, A nonlinear viscoelastic model of lung tissue mechanics, Journal of Applied Physiology 71 (3) (1991) 826–833.

[222] D. E. Hurtado, N. Avilés-Rojas, F. Concha, Multiscale modeling of lung mechanics: From alveolar microstructure to pulmonary function, Journal of the Mechanics and Physics of Solids (2023) 105364.