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A Reactive Inelasticity Theoretical Framework for Modeling Viscoelasticity, Plastic Deformation, and Damage in Fibrous Soft Tissue

Fibrous soft tissues are biopolymeric materials that are made of extracellular proteins, such as different types of collagen and proteoglycans, and have a high water content. These tissues have nonlinear, anisotropic, and inelastic mechanical behaviors that are often categorized into viscoelastic behavior, plastic deformation, and damage. While tissue's elastic and viscoelastic mechanical properties have been measured for decades, there is no comprehensive theoretical framework for modeling inelastic behaviors of these tissues that is based on their structure. To model the three major inelastic mechanical behaviors of tissue's fibrous matrix, we formulated a structurally inspired continuum mechanics framework based on the energy of molecular bonds that break and reform in response to external loading (reactive bonds). In this framework, we employed the theory of internal state variables (ISV) and kinetics of molecular bonds. The number fraction of bonds, their reference deformation gradient, and damage parameter were used as state variables that allowed for consistent modeling of all three of the inelastic behaviors of tissue by using the same sets of constitutive relations. Several numerical examples are provided that address practical problems in tissue mechanics, including the difference between plastic deformation and damage. This model can be used to identify relationships between tissue's mechanical response to external loading and its biopolymeric structure. [DOI: 10.1115/1.4041575]

1 Introduction

Fibrous soft tissues, such as tendon, meniscus, intervertebral disk, etc., are biopolymeric materials that have nonlinear, anisotropic, and inelastic mechanical behaviors. An inelastic behavior, contrary to an elastic behavior, is one that dissipates energy during mechanical loading. Three major inelastic behaviors that are experimentally observed in fibrous soft tissues are viscoelastic behavior [1–3], plastic deformation [4–7], and damage [8,9]. Understanding the underlying mechanisms of these behaviors is essential for elucidating the relationships among the mechanical loading, pathological conditions (e.g., tendinopathy, meniscus rupture, and disk herniation), and tissue's structure.

Fibrous soft tissues have a hierarchical structure that is predominantly composed of extracellular proteins, such as different types of collagen and proteoglycans, and have a high water content, where the underlying microstructural organization is responsible for the variations in tissue's mechanical properties. Inelastic mechanical responses can occur with loading, resulting in altered microstructure and mechanical properties, and even loss of function and rupture. While tissue's elastic and viscoelastic behaviors have been studied for decades, there is no comprehensive framework for studying inelastic behaviors of tissue in a structural context; perhaps due to the complex nature of experimental measurement of the inelastic behaviors that occur simultaneously and can have overlapping effects (e.g., plastic deformation and damage). Thus, a theoretical framework is necessary to study these behaviors that uniquely identify characteristics of different inelastic behaviors and their underlying mechanisms based on tissue structure.

From a theoretical point of view, an inelastic behavior is a path-dependent and irreversible thermodynamic process that may be modeled using the theory of internal state variables (ISV) [10,11]. Various phenomenological ISV expressions have been used to model tissue's mechanical behavior. For instance, decomposition of strain [12] and stress [13] tensors into elastic and inelastic components is a common practice to model viscoelasticity, where the inelastic components are hidden internal variables that correspond to the nonequilibrium part of the mechanical response. For plastic deformation (permanent set) in tissue, Zhang and Sacks [14] used a structural approach to model this inelastic behavior in cyclic loading by proposing a shift in reference configuration of exogenously crosslinked matrix. In another study, to model softening based on permanent set and damage, two weight factors were used based on alterations to the fibrous structure of tissue due to mechanical loading [15,16]. A similar inelastic variable set was used to model permanent deformation and damage that evolve according to the history of maximum energy of fiber families [17] that is based on the theory of *pseudo-elasticity* [18,19]. Damage, perhaps the most common variable for modeling tissue inelasticity [20], is often used to model stress-softening or Mullin's effect [21,22]. In tissue, damage is usually modeled according to the number of "broken" fibers [8,23,24]. This formulation is similar to the definition of the damage parameter in classic continuum damage mechanics that is based on occurrence of microvoids in engineering material such as metals and concrete [25,26]. Despite nearly four decades of successful use of phenomenological approaches to study tissue's inelastic behaviors, their applicability is limited by the focus of individual models on a subset of inelastic behaviors, and in particular for ISV approaches, there is often not a clear physical interpretation of parameters.

In this study, we used the combination of the theory of ISVs and the kinetics of molecular bonds to develop a structurally inspired continuum mechanics framework that addresses the

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inelastic behaviors of tissue's solid matrix. In a few words, we define reactive bonds as those which break and reform in response to mechanical loading; this process results in dissipative changes to the stored energy of the material and inelastic mechanical behaviors. We selected the number fraction of molecular bonds (w^α), their reference deformation gradient (Π^α), and damage parameter (D) as state variables to address inelastic behaviors. This framework allows for modeling of all three of the aforementioned inelastic behaviors (viscoelastic behavior, plastic deformation, and damage) using the same set of constitutive relations at different ranges of kinetic rates of bond breakage and reformation.

Kinetics of molecular bonds has been previously introduced by Tobolsky and co-workers to model stress-relaxation of polymers based on the energy of a network of molecules with transient cross-links, that is commonly referred to as the *two-network model* [27,28]. In a similar way, permanent set has been modeled using the idea of kinetics of breaking and reforming bonds [29,30], where often the concept of a material with multiple natural configurations is employed in a thermomechanical framework [31,32]. This framework is widely used for studying mechanical behaviors of engineering polymers [33–37] with various physical interpretations based on the molecular structure of polymers [22]. For tissue mechanics applications, a similar idea was recently adapted to model damage of cartilaginous constructs that addresses damage as the fraction of failed bonds, which is an observable variable and can be experimentally measured [38]. Reactive viscoelasticity was introduced by Ateshian to model viscoelasticity of a constrained solid mixture [39,40]. In that model, two separate bond types were introduced: weak and strong, to model the transient and equilibrium mechanical response, respectively. In the current work, we generalize that concept and show that these bonds are not separate, and strong bonds are a special case of weak bonds. Additionally, by employing this generalization and taking inspiration from prior work in polymer mechanics, the sliding bond type was introduced that can instantaneously break and reform into a stressed-configuration, which results in plastic deformation. Given the structural basis of this framework and its consistency in addressing several inelastic behaviors, reactive inelasticity is well suited for studying the underlying mechanisms of inelasticity in tissue. Thus, the objective of this study was to comprehensively address tissue inelasticity by developing a structurally inspired continuum mechanics framework, reactive inelasticity (RIE), based on the energy of reactive molecular bonds.

This paper is organized as follows: in Sec. 2, we formulate the theory of reactive inelasticity by defining the free energy of a reactive body with generic molecular bond types, where the concepts of intrinsic hyperelasticity and generalized bond kinetics are formulated. Further, we introduce special bond types suited for

different mechanical behaviors: formative bonds for viscoelastic behavior, permanent bonds for hyperelastic behavior, and sliding bonds for plastic deformation. Damage is added to the formulation by allowing for the reduction of the number fraction of bonds. To demonstrate the key features of this framework, in Sec. 3 we provide several numerical examples of the mechanical behavior of single bond types and their combinations. Finally, in Sec. 4, comparisons to the other existing inelasticity models for tissue and physical interpretation of bonds are discussed.

2 Reactive Inelasticity

In the following, we will describe the mechanics of a reactive material. A reactive material is made of a combination of different bond types each with different characteristics. Each bond type is associated with a certain mechanical behavior (e.g., formative bonds with viscoelastic behavior). Bonds break and reform (i.e., react) when subjected to an external loading and this process initiates new generations. Generations are molecular bonds of certain bond type that were initiated at the same time and, thus, have a mutual reference configuration. Damage is introduced to all of the bond types by reducing the fraction of bonds in the material, and finally the consequences of the second law of thermodynamics are discussed.

2.1 Kinematics and Relative Deformation. Consider a solid body made of a set of material points that are energetically constrained with different types of molecular bonds (indicated by a subscript γ). These bonds deform in a smooth path $\mathbf{x} := \chi(\mathbf{X}, t)$, where $\mathbf{x}$ stands for the current configuration of bonds and $\mathbf{X}$ is their master reference configuration. Hence, the deformation gradient tensor is defined as $\mathbf{F} := \partial\chi(\mathbf{X}, t)/\partial\mathbf{X}$ and the right Cauchy–Green deformation tensor as $\mathbf{C} := \mathbf{F}^T \mathbf{F}$. Each bond type may have different generations (indicated by superscript α), and despite their mutual path of deformation and master reference configuration, every generation has a different reference configuration ($\mathbf{X}^\alpha$), which is a function of the conditions at the time of formation of the bonds (Fig. 1). By using the chain rule of differentiation, the relative deformation gradient tensor for each generation ($\mathbf{F}_\gamma^\alpha$) is

$$\mathbf{F}_\gamma^\alpha := \mathbf{F}(\Pi_\gamma^\alpha)^{-1} \quad (1)$$

where $\Pi_\gamma^\alpha := \partial\mathbf{X}^\alpha/\partial\mathbf{X}$ is the reference deformation gradient tensor of generation α of bond type γ . This procedure results in *multiplicative decomposition* of deformation [41–43]. As a result, the relative right Cauchy–Green deformation tensor $\mathbf{C}_\gamma^\alpha$ is

$$\mathbf{C}_\gamma^\alpha := (\Pi_\gamma^\alpha)^{-T} \mathbf{C} (\Pi_\gamma^\alpha)^{-1} \quad (2)$$

note that $\mathbf{A}^{-T} := (\mathbf{A}^{-1})^T$.

2.2 Free Energy and Intrinsic Hyperelasticity. The free energy density of the system is the combination of the energy density of all the bond types

$$\Psi = \sum_\gamma \Psi_\gamma \quad (3)$$

where Ψ is the Helmholtz free energy density (per volume). The energy density of each bond type is the sum of the energy from each of its generations

$$\Psi_\gamma = \sum_\alpha n_\gamma^\alpha \bar{\psi}_\gamma^\alpha \quad (4)$$

where n_γ^α is the number density, and $\bar{\psi}_\gamma^\alpha$ is the average energy of bonds from generation α of bond type γ . Alternatively, by defining the number fraction of each generation as

Fig. 1 Reference configuration of generations: in a body with the master reference configuration $\mathbf{X}$ for generation α the relative deformation gradient tensor ($\mathbf{F}^\alpha$) is defined using the reference configuration ($\mathbf{X}^\alpha$)

$$w_\gamma^\alpha = \frac{n_\gamma^\alpha}{\sum_\alpha n_\gamma^\alpha} = \frac{n_\gamma^\alpha}{n_{\gamma,\text{total}}} \quad (5)$$

where $n_{\gamma,\text{total}}$ is the number density of a bond type in the natural state of the material, Eq. (4) can be rewritten as

$$\Psi_\gamma = \sum_\alpha w_\gamma^\alpha \psi_\gamma^\alpha \quad (6)$$

where

$$\psi_\gamma^\alpha = n_{\gamma,\text{total}} \bar{\psi}_\gamma^\alpha \quad (7)$$

Here, ψ_γ^α denotes the overall energy density of a generation, which, in general, can be a function of deformation, temperature, and other state variables. However, in this formulation we consider a unique deformation dependence that implies that generations are *intrinsically hyperelastic*. That is,

$$\psi_\gamma^\alpha = \psi_\gamma(C^\alpha) \quad (8)$$

The previous equation also denotes that the intrinsic hyperelasticity relation is the same for all of the generations of one bond type, and thus is a characteristic of that type of bond. Therefore, Eq. (6) reads as

$$\Psi_\gamma = \sum_\alpha w_\gamma^\alpha \psi_\gamma(C_\gamma^\alpha) \quad (9)$$

Note that for a bond type with no damage

$$\sum_\alpha w_\gamma^\alpha = 1 \quad (10)$$

which indicates that the energy density of each bond type (Eq. (9)) is a weighted sum of the energy density of all its generations. Thus, the overall free energy density of the material can be written in the following form:

$$\Psi(\mathbf{F}, w_\gamma^\alpha, \mathbf{\Pi}_\gamma^\alpha) = \sum_\gamma \sum_\alpha w_\gamma^\alpha \psi_\gamma(C_\gamma^\alpha) \quad (11)$$

Here, deformation (represented by $\mathbf{F}$), the number fraction of generations of bond types (w_γ^α), and their reference deformation gradient ($\mathbf{\Pi}_\gamma^\alpha$) are the state variables. To simplify the notation without losing generality, we will continue the discussion for one type of bond, where the total response for a mixture of multiple bond types should be taken as a summation over all existing bond types (such as in Eq. (11)).

The second Piola–Kirchhoff stress tensor is written as [10]

$$\mathbf{S}(\mathbf{F}, w_\gamma^\alpha, \mathbf{\Pi}_\gamma^\alpha) = 2 \frac{\partial \Psi(\mathbf{F}, w_\gamma^\alpha, \mathbf{\Pi}_\gamma^\alpha)}{\partial \mathbf{C}} \quad (12)$$

Also, by using Eq. (9) for a reactive material, Eq. (12) can be rewritten as (see the Supplementary document which is available under the “[Supplemental Data](#)” tab for this paper on the ASME digital collection)

$$\mathbf{S}(\mathbf{F}, w^\alpha, \mathbf{\Pi}^\alpha) = \sum_\alpha w^\alpha (\mathbf{\Pi}^\alpha)^{-1} \mathbf{S}^\alpha(C^\alpha) (\mathbf{\Pi}^\alpha)^{-T} \quad (13)$$

where we also adopted the following definition for stress associated with each generation:

$$\mathbf{S}^\alpha(C^\alpha) := 2 \frac{\partial \psi(C^\alpha)}{\partial \mathbf{C}^\alpha} \quad (14)$$

For coordinate-invariance, the state of stress equivalently is determined using the invariants of $\mathbf{C}^\alpha$

$$I_1^\alpha = \text{tr}(\mathbf{C}^\alpha), \quad I_2^\alpha = \frac{1}{2} [\text{tr}(\mathbf{C}^\alpha)^2 - \text{tr}((\mathbf{C}^\alpha)^2)], \text{ and } I_3^\alpha = \det(\mathbf{C}^\alpha) \quad (15)$$

where $\text{tr}(\cdot)$ and $\det(\cdot)$ stand for trace and determinant of a second-order tensor, respectively. Often, the given set of invariants suffices to describe the state of deformation; however, it is customary to add additional *pseudo invariants* for anisotropic material (e.g., tendon, and ligament). A common pseudoinvariant for transversely isotropic material is defined as [44,45]

$$I_4^\alpha := \mathbf{M}^\alpha : \mathbf{C}^\alpha \quad (16)$$

In this equation, $\mathbf{M}^\alpha$ is a second-order structure tensor defined as

$$\mathbf{M}^\alpha := \mathbf{e}_\gamma^\alpha \otimes \mathbf{e}_\gamma^\alpha, \text{ where } \mathbf{e}_\gamma^\alpha := \frac{\mathbf{\Pi}^\alpha \mathbf{e}_\gamma^0}{\|\mathbf{\Pi}^\alpha \mathbf{e}_\gamma^0\|} \quad (17)$$

Here, $\mathbf{e}_\gamma^\alpha$ is a unit vector on the dominant fiber direction in the generation α reference configuration. Therefore, the second Piola–Kirchhoff stress ($\mathbf{S}$) in terms of deformation invariants reads as

$$\mathbf{S}(\mathbf{F}, w^\alpha, \mathbf{\Pi}^\alpha) = \sum_\alpha w^\alpha (\mathbf{\Pi}^\alpha)^{-1} \left(\sum_{i=1}^4 2 \frac{\partial \psi}{\partial I_i^\alpha} \frac{\partial I_i^\alpha}{\partial \mathbf{C}^\alpha} \right) (\mathbf{\Pi}^\alpha)^{-T} \quad (18)$$

where the derivatives of the deformation invariants are

$$\frac{\partial I_1^\alpha}{\partial \mathbf{C}^\alpha} = \mathbf{I}, \quad \frac{\partial I_2^\alpha}{\partial \mathbf{C}^\alpha} = I_1^\alpha \mathbf{I} - \mathbf{C}^\alpha, \quad \frac{\partial I_3^\alpha}{\partial \mathbf{C}^\alpha} = I_3^\alpha (\mathbf{C}^\alpha)^{-1}, \text{ and } \frac{\partial I_4^\alpha}{\partial \mathbf{C}^\alpha} = \mathbf{M}^\alpha \quad (19)$$

The Cauchy stress ($\mathbf{T}$) is then obtained from the second Piola–Kirchhoff stress (Eq. (18)) as $\mathbf{T} = J^{-1} \mathbf{F} \mathbf{S} \mathbf{F}^T$, where $J = \det(\mathbf{F})$. By using the relative deformation gradient tensor, defined earlier in Eq. (1), the Cauchy stress tensor for each bond type is

$$\mathbf{T}(\mathbf{F}, w^\alpha, \mathbf{\Pi}^\alpha) = \frac{1}{J} \sum_\alpha w^\alpha \mathbf{F}^\alpha \left(\sum_{i=1}^4 2 \frac{\partial \psi}{\partial I_i^\alpha} \frac{\partial I_i^\alpha}{\partial \mathbf{C}^\alpha} \right) (\mathbf{F}^\alpha)^T \quad (20)$$

and by defining the contribution of each generation ($\mathbf{T}^\alpha$) as [37]

$$\mathbf{T}^\alpha(\mathbf{F}^\alpha) := \mathbf{F}^\alpha \left(\sum_{i=1}^4 2 \frac{\partial \psi}{\partial I_i^\alpha} \frac{\partial I_i^\alpha}{\partial \mathbf{C}^\alpha} \right) (\mathbf{F}^\alpha)^T \quad (21)$$

the Cauchy stress tensor for a specific bond type reads as

$$\mathbf{T}(\mathbf{F}, w^\alpha, \mathbf{\Pi}^\alpha) = \frac{1}{J} \sum_\alpha w^\alpha \mathbf{T}^\alpha(\mathbf{F}^\alpha) \quad (22)$$

Similar to energy, the previous equation indicates that the Cauchy stress of a bond type is the weighted sum of the contributions from all the generations of that bond type.

So far, we have described the fundamental formulation for states of energy and stress in terms of state variables ($\mathbf{F}, w^\alpha, \mathbf{\Pi}^\alpha$). In the following sections, we will describe the energy relations and kinetics of bonds to describe the states of energy and stress in a reactive material.

2.3 Reactive Bond Kinetics. In general, the reactive bonds break and reform (react) when subjected to loading. This process produces the evolution of the states of energy and stress (Eqs. (11) and (22)). As an example, for a system with one type of bond, after a unit step deformation the bonds start breaking and their number fraction (w^0) starts to decrease (Fig. 2). Simultaneously,

Fig. 2 Example of bonds with first-order rate equation: after a step deformation at $t=0$, the bonds start to break (w^0), and simultaneously reform to a new state (w^1). With no further loading, all the bonds eventually break and reform to the new configuration as $t \rightarrow \infty$ (in this example, $\tau = 10$).

the broken bonds reform to a new state, initiating a new generation, where the number fraction of this new generation (w^1) increases over time. In the absence of damage, according to Eq. (10) the sum of the number fraction of the breaking and reforming bonds is one (i.e., $w^0(t) + w^1(t) = 1$). As a result, the free energy for a step deformation is

$$\Psi(F, w^0, w^1, \Pi^0, \Pi^1) = w^0(t)\psi(C^0) + w^1(t)\psi(C^1) \quad (23)$$

If the bonds reform in a stress-free fashion ($C^1 = I$), without further loading all of the energy would be dissipated. That is,

$$\dot{\Psi} = \dot{w}^0(t)\psi(C^0) < 0, \quad \text{and} \quad \lim_{t \rightarrow \infty} \Psi = 0 \quad (24)$$

where the dot-notation stands for time derivative. To determine the rate of breakage of bonds, a kinetics rate equation is used. The general form of the kinetics rate equation may be written as

$$\dot{w}^\alpha = \Upsilon(w^\alpha, \Gamma_i) \quad (25)$$

In this equation, $\Upsilon(\cdot)$ is a negative-valued function of the available reactants (breaking bonds of w^α) and other state variables such as relative deformation ($\Gamma = F^z$) [39], temperature ($\Gamma = \theta$) [35], or for polymeric macro molecules, geometrical characteristics of bonds such as the end-to-end distance and directional angles [36,46]. Despite features that can be added to the rate equation, there are general conditions that need to be satisfied. First, any rate equation should not result in a negative number fraction for any bond generation. Second, it should induce a breaking bond number fraction that asymptotically decays to zero in the limit of infinite time. In this paper, we used the first-order relation, which is the simplest form of a kinetics rate equation satisfying conditions

$$\dot{w}^\alpha = -\frac{1}{\tau} w^\alpha \quad (26)$$

In the previous equation, τ is the time constant of reaction that controls the rate of breakage and reformation. When multiple consecutive steps of deformation occur at $t^\alpha \in \{t^0, t^1, t^2, \dots, t^n\}$, the number fraction resulting from each deformation for this first-order system is (Fig. 3(a)) [39]

$$w^\alpha(t) = \begin{cases} f^\alpha(t) & t^\alpha < t \leq t^{\alpha+1} \\ f^\alpha(t^{\alpha+1}) \exp(-(t - t^{\alpha+1})/\tau) & t^{\alpha+1} < t \end{cases} \quad (27)$$

In this relation, $f^\alpha(t) = 1 - \sum_{(x; t^x < t)} w^\alpha(t)$ according to Eq. (10) that describes the reformation of bonds. The dependence of the rate of breakage on the number fraction of breaking bonds results in an asymptotic exponential decay of bonds. Note that Eq. (27) can only be used for first-order kinetics with nonvarying time-constant, and for a general rate equation, the number fraction of bonds is numerically calculated from Eqs. (10) and (25).

2.4 Bond Types. The state of energy (Eq. (11)) for a given bond type depends on the number fraction (w^α) of bonds and their reference deformation gradient (Π^α). To characterize the

Fig. 3 Consecutive step deformations and multiple generations: ((a)–(c)) number fraction of multiple generations initiated at four consecutive step deformations at $t = 0, 15, 30, 45$ with a first-order rate equation, and ((d)–(f)) their corresponding reference deformation gradients. ((a), (d)) Formative bonds ((b), (e)) permanent bonds ((c), (f)) sliding bonds. For the number fraction graphs ((a)–(c)), the sum of all of the generations is shown with a horizontal green dashed line. The deformation stretch is shown with a red dashed line on reference configuration graphs. Note that Π^α in general is a second-order tensor, and we used a one-dimensional representative for more convenient illustration ((d)–(f)).

evolution of these variables, we define three types of bonds: (1) formative; (2) permanent; and (3) sliding to address viscoelasticity, hyperelasticity, and plastic deformation, respectively.

2.4.1 Formative Bonds. These bonds have a time constant that is on the order of the characteristic time (t_c) of the experimental observation. That is, $\tau_f/t_c \approx 1$, where $\gamma = f$ stands for formative bond type (Fig. 3(a)). The reference deformation gradient of the new generations of bonds is defined at the current configuration at the time the bonds were initiated (Fig. 3(d))

$$\Pi_f^\alpha = \mathbf{F}(t^\alpha) \quad (28)$$

Equivalently, for two consecutive generations

$$\Pi_f^\alpha = \Pi_f^{\alpha-1} + u(t - t^\alpha)(\mathbf{F}(t^\alpha) - \mathbf{F}(t^{\alpha-1})) \quad (29)$$

where $u(\cdot)$ is the unit step function. In this case, during a sustained deformation the energy and stress of the system asymptotically decays as the bonds break, resulting in a fluid-like behavior; a transient viscoelastic mechanical response with zero equilibrium stress.

2.4.2 Permanent Bonds. Permanent bonds represent a special case of kinetics rate, where the rate of breakage of bonds is extremely slow ($\tau_p/t_c \rightarrow \infty$, $\gamma = p$) (Fig. 3(b)). As a result, only one generation of bonds exists ($w_p^0 = 1$) and the reference deformation gradient of that generation is (Fig. 3(e))

$$\Pi_p^\alpha = \mathbf{I} \quad (30)$$

Since the bonds are intrinsically hyperelastic (Eqs. (8) and (14)), the overall behavior of permanent bonds is hyperelastic, where the states of energy and stress are independent of the history of deformation.

2.4.3 Sliding Bonds. Sliding bonds represent another special case, where the rate of breakage and reformation of bonds is extremely fast compared to the characteristic time ($\tau_s/t_c \rightarrow 0$, $\gamma = s$) (Fig. 3(c)). In this case, if the bonds could reform to the current configuration, all the energy would immediately be dissipated. If the newly formed bonds have a different reference deformation gradient Π_s^α than the current configuration, they slide (Fig. 3(f)). This implies that the bonds are reforming in a loaded state, and only part of the energy is used for the sliding process and the rest is stored. Since Π_s^α is a state variable, by selecting appropriate constitutive relations the sliding process can be made to produce plastic deformation.

The evolution of Π_s^α is governed by a set of constitutive relations. Following from the classical theory of plasticity [47,48], we formulated the evolution of the sliding reference deformation gradient using a sliding condition and sliding rule in a rate-independent formulation. Similar to Eq. (29), the sliding process is incremental from one generation to the next, i.e.,

$$\Pi_s^\alpha(t) = \Pi_s^{\alpha-1}(t^\alpha) + u(t - t^\alpha)\Delta\Pi_s^\alpha \quad (31)$$

where $\Delta\Pi_s^\alpha$ is an incremental infinitesimal change to the reference deformation gradient due to sliding. Note that the zeroth generation's reference deformation gradient is the identity tensor ($\mathbf{I} = \mathbf{e}_i \otimes \mathbf{e}_i$). Although the change is infinitesimal, it does not imply that Π_s^α is infinitesimal or that the incremental nature of the sliding process goes away, no matter how small the sliding would be.

The sliding only occurs when the sliding condition is met. Otherwise, bonds do not break and due to intrinsic hyperelasticity assumption they behave similarly to permanent bonds. The sliding condition (analogous to yield condition) is defined as

$$\varphi_s(\Xi_s, r_s) := \Xi_s - r_s \leq 0 \quad (32)$$

where Ξ_s is the sliding variable and r_s is the sliding threshold, where all are scalar. The sliding variable is a function of deformation, or equivalently the invariants of deformation

$$\Xi_s = \hat{\Xi}_s(\mathbf{C}) \equiv \hat{\Xi}_s(I_1, I_2, I_3, I_4) \quad (33)$$

The sliding threshold r_s is defined as the maximum value of Ξ_s obtained in the history of deformation [49]

$$r_s := \max \left\{ (r_0)_s, \max_{\tilde{t} \in (-\infty, t]} \Xi_s(\tilde{t}) \right\} \quad (34)$$

The initial value of r_s before any loading is the initial sliding threshold denoted by $(r_0)_s$, which is a material property. Equations (32) and (34) indicate $\varphi_s(\Xi_s, r_s) \leq 0$, which corresponds to the physically admissible deformations [47]. Sliding can only be initiated when $\varphi_s = 0$ (necessary condition). To determine the sufficient condition, we need to include the loading direction by defining the second-order tensorial normal to the sliding surface ($\varphi_s = 0$)

$$\mathbf{N}_s := \left. \frac{\partial \varphi_s}{\partial \mathbf{C}} \right|_{\varphi_s=0} \quad (35)$$

While the necessary condition for sliding is in place, two scenarios of loading can occur [50]

$$\begin{cases} \mathbf{N}_s : \dot{\mathbf{C}} \leq 0 & \text{(no sliding)} \\ \mathbf{N}_s : \dot{\mathbf{C}} > 0 & \text{(sliding)} \end{cases} \quad (36)$$

where only the second scenario can initiate a sliding behavior. Here, $\dot{\mathbf{C}}$ is the material time derivative of the right Cauchy–Green deformation tensor $\dot{\mathbf{C}} := \mathbf{F}^T(\dot{\mathbf{F}}\mathbf{F}^{-1} + \mathbf{F}^{-T}\dot{\mathbf{F}}^T)\mathbf{F}$. When the necessary and sufficient conditions of sliding ($\varphi_s = 0$ and $\mathbf{N}_s : \dot{\mathbf{C}} > 0$) are in place, the incremental sliding can be calculated using the sliding rule

$$\Delta\Pi_s^\alpha = \mathbf{R}(\mathbf{F}, \Pi_s^{\alpha-1}) \quad (37)$$

where $\mathbf{R}$ is a second-order tensor function. An example of sliding rule for a medium with a dominant fiber direction would be

$$\Delta\Pi_s^\alpha = \frac{\partial f_s(\Xi_s)}{\partial \Xi_s} \Delta\Xi_s \tilde{\mathbf{M}}^\alpha \quad (38)$$

where f_s is the sliding function, $\Delta\Xi_s$ is the difference between sliding variables of two consecutive generations involved in the sliding process (Eq. (31)), and $\tilde{\mathbf{M}}^\alpha$ is a second-order structure tensor. To define $\tilde{\mathbf{M}}^\alpha$ it was assumed that the initial dominant fiber orientation is preserved in the sliding configurations, i.e., $\mathbf{e}^\alpha = \lambda_s^\alpha \mathbf{e}^0$. Therefore, one can show (see the Supplementary document which is available under the “Supplemental Data” tab for this paper on the ASME digital collection)

$$\tilde{\mathbf{M}}^\alpha = \mathbf{e}^0 \otimes \mathbf{e}^0 \quad (39)$$

This particular constitutive relation indicates that the configuration of increments of sliding depends on the extent of deformation and the orientation of bonds in the master reference configuration. As another example, for three-dimensional (3D) cases where an analytical expression is available for $\mathbf{F}$, one can choose $\Pi_s^\alpha = \mathbf{F}(\lambda_s^\alpha)$ [30]. In general, however, for finite strain plastic deformation an analytic expression is not available, and one should use the well-established theory of finite-strain plasticity to formulate the intermediate configuration [41,51,52].

For completeness, because the reference configuration is time invariant after formation of bonds and the sliding process is incremental (Eq. (31)), the rate of sliding for each reforming bond generation is determined using

Table 1 Summary of structure of a reactive bond type's constitutive relations

Step 1	Select the bond types (i.e., formative, permanent, sliding)
Step 2	Select the kinetics relation (e.g., Eq. (26))
Step 3	Select the intrinsic hyperelasticity relation $\psi_\gamma(C^\alpha)$ (e.g., neo-Hookean)
Step 4	If sliding bonds, select appropriate constitutive relations: Sliding variable (Ξ_s) (Eq. (33)) Sliding rule and function (f_s) (Eq. (38))
Step 5	If damage is included, select appropriate constitutive relations: Damage variable (Ξ_D) (Eq. (44)) Damage rule and function (f_D) (Eq. (48))

$$\dot{\Pi}_s^\alpha = \delta(t - t^\alpha) \Delta \Pi_s^\alpha(t^\alpha) \quad (40)$$

where $\delta(\cdot)$ is the Dirac delta function that denotes the incremental nature of sliding process. This relation will be helpful later in the analysis of the second law of thermodynamics (Sec. 2.6).

2.5 Damage of Bonds. Damage is an irreversible process that is due to a loss of chemical bonds [53]. This is often observed as a softening behavior that is also referred to as Mullin's effect [21]. The idea of relating damage to molecular bonds in tissue can be traced back as early as Ref. [54] for modeling the hysteresis effect. In the current framework, damage of the various bonds (D) was considered as another state variable, where with a damaging load, the broken bonds may not be reformed, which, in turn, decreases the number of active bonds. That is,

$$\left(\sum_\alpha w^\alpha \right)_{\text{Damaged}} = (1 - D) \sum_\alpha w^\alpha \quad (41)$$

where D is the damage parameter of a certain bond type and it takes a value between zero and one ($D \in [0, 1]$) [38]. Damage can be applied to each of the bond types (Fig. 4). By doing so, the total energy of the bonds decreases as the number fraction of damaged bonds increases. Hence, the free energy is

$$\Psi(F, w^\alpha, \Pi^\alpha, D) = (1 - D) \sum_\alpha w^\alpha \psi(C^\alpha) \quad (42)$$

which always has a value less than the nondamaged case.

To determine the evolution of damage, similar to the sliding case, the damage condition is defined as

$$\varphi_D(\Xi_D, r_D) := \Xi_D - r_D \leq 0 \quad (43)$$

Here, Ξ_D is the damage variable that is a function of deformation invariants

$$\Xi_D = \hat{\Xi}_D(C) \equiv \hat{\Xi}_D(I_1, I_2, I_3, I_4) \quad (44)$$

and r_D is the damage threshold defined as the maximum value of Ξ_D in the past history of deformation [49]. The damage threshold r_D is defined separately for each bond type as

$$r_D := \max \left\{ (r_0)_D, \max_{\tilde{t} \in (-\infty, t]} \Xi_D(\tilde{t}) \right\} \quad (45)$$

The value of r_D before any loading is the initial damage threshold $((r_0)_D)$, which is a material property. Damage occurs when $\varphi_D = 0$ (necessary condition). The loading direction determines the sufficient conditions. By defining the second-order tensorial normal to the damage surface ($\varphi_D = 0$) as

$$N_D := \frac{\partial \varphi_D}{\partial C} \bigg|_{\varphi_D=0} \quad (46)$$

and by using the following normality conditions [49]:

$$\begin{cases} N_D : \dot{C} \leq 0 & (\text{no damage}) \\ N_D : \dot{C} > 0 & (\text{damage}) \end{cases} \quad (47)$$

damage only occurs when ($\varphi_D = 0$ and $N_D : \dot{C} > 0$). Thus, during a damaging load, the damage parameter increases according to the damage rule

$$\dot{D} = \frac{\partial f_D(\Xi_D)}{\partial \Xi_D} \dot{\Xi}_D \quad (48)$$

where $f_D(\Xi_D)$ is the damage function. Note that the damage variable (Ξ_D) is different from damage parameter (D), where D is the number fraction of permanently broken bonds.

2.6 Implications of the Second Law of Thermodynamics.

As a consequence of the second law (as shown in detail in the Supplementary document S.3 which is available under the "Supplemental Data" tab for this paper on the ASME digital collection), the bonds are "second-law compatible" if appropriate constitutive relations are used. Formative and permanent bonds are second-law compatible when appropriate kinetics relation is used, and for sliding bonds, the change in reference configuration (Eq. (38)) needs to be defined so as to satisfy positive dissipation of energy (Supplementary document S.3 which is available under the "Supplemental Data" tab for this paper on the ASME digital collection). For damage, f_D (Eq. (48)) needs to be selected to guarantee $\dot{D} \geq 0$ (e.g., cumulative distribution function of a continuous statistical distribution). Examples of appropriate constitutive relations will be provided in Sec. 3.

2.7 Summary of Formulation. In summary, a reactive inelasticity model was formulated that defines different types of bonds corresponding to different mechanical behaviors. The combination of bond types should be selected according to the observed mechanical behaviors (as described in Sec. 2.4). In

Fig. 4 Effect of damage on kinetics: multiple generations initiated at four consecutive step deformations at $t = 0, 15, 30, 45$ with a first-order rate equation with damage shown for (a) formative bonds (b) permanent bonds and (c) sliding bonds, the sum of bonds declines after each step of loading until the final value of 0.75 ($D = 0.25$)

Fig. 5 Example 1: time response of formative bonds to a Heaviside step deformation in a large range of kinetics. The kinetics rate is controlled by time constant of reaction where $(\tau_f)_0 = 10$ and the range of time constants is covered by multiplying $(\tau_f)_0$ with powers of two. Formative bonds show an asymptotic decay in Cauchy stress during a sustained loading, whereas for large values of τ_f (slow kinetics rate) the response approaches a hyperelastic behavior (permanent bonds) marked with dashed line, and at small τ_f (high kinetics rate), the stress response approaches a singular behavior that is immediately decays to zero (sliding bonds). The step deformation is $\lambda(t) = 1.1u(t)$ and the neo-Hookean intrinsic hyperelasticity parameter is $C_1 = 100$.

selecting the constitutive relations, it is perhaps more convenient to take the discrete steps that are outlined in Table 1. In the following section, several illustrative examples are provided that both help in understanding the model and also to exemplify some practical applications to mechanics of soft tissue, where reactive inelasticity can be useful.

3 Illustrative Examples

To demonstrate key features of the RIE framework, we provide three numerical examples. First, the sensitivity of formative bonds to the kinetics rate is demonstrated using a Heaviside step loading that shows transitions between different bond types (example 1). Second, we simulate the stress response of an increasing cyclic loading by using a fiber-exponential constitutive relation that is commonly used in tissue mechanics, and we compare the stress response between nondamaged and damaged cases (example 2). Finally, incremental stress relaxation with softening is presented for an anisotropic case, which has importance to understand mechanisms of plastic deformation and damage in tissue. This is done by using a combination of formative bonds and either sliding bonds or permanent bonds with damage (example 3). The model is implemented as a MATLAB function using a custom written code intended for uniaxial deformations. The source code and details of implementation are provided as Supplementary material and are accessible online.²

For all of the examples, the axial component of the Cauchy's stress tensor (i.e., $T = T_{33}$) was used to represent the state of stress during a uniaxial isochoric deformation

$$\mathbf{F} = \hat{\mathbf{F}}(\lambda(t)) := e_i \otimes e_i \frac{1}{\sqrt{\lambda}} + e_3 \otimes e_3 \left(\lambda - \frac{1}{\sqrt{\lambda}} \right) \quad i = 1, 2, 3 \quad (49)$$

The following constitutive relations were implemented in the steps outlined in Table 1:

- **Step 1-Bond type selection:** The bond type was selected depending on the expected mechanical behavior. Formative bonds were used for a viscoelastic behavior with zero equilibrium stress, permanent bonds for a hyperelastic behavior,

and sliding bonds were used for plastic deformation. Note that for example 3, which includes a combination of bonds, the response was calculated independently for each bond type and added according to Eq. (11).

- **Step 2-Kinetics relation:** For all of the examples, a first-order kinetics relation was used (Eq. (26)).
- **Step 3-Intrinsic hyperelasticity:** Three types of nonlinear constitutive relations were used. First, we used the neo-Hookean relation in example 1. This is the simplest nonlinear constitutive relation and was used to demonstrate the general behaviors of the model, where the potential energy is

$$\psi_{\text{NH}}(I_1) = C_1(I_1 - 3) \quad (50)$$

Here, C_1 is the independent model parameter with dimensions of stress.

Second, for relevance to tissue applications, in examples 2 and 3, we used a one-dimensional exponential constitutive relation with a nonzero stiffness only in the e_3 direction (fiber direction) in tension [23,55]

$$\psi_{\text{EF}}(I_4) = C_2 \left(\exp \left[C_3(I_4 - 1)^2 \right] - 1 \right) u(I_4 - 1) \quad (51)$$

where C_2 and C_3 are positive-valued model parameters.

Third, for showing a three-dimensional tissue mechanics application, we used a Holmes–Mow material (example 3)

$$\psi_{\text{HM}}(I_1, I_2, I_3) = \alpha_0 \left(I_3^{-\beta} \exp [\alpha_1(I_1 - 3) + \alpha_2(I_2 - 3)] - 1 \right) \quad (52)$$

In this relation, α_0 is a positive number with the dimension of stress and $[\beta, \alpha_1, \alpha_2]$ are positive nondimensional numbers. To comply with the energy- and stress-free reference configuration, $\beta = \alpha_1 + 2\alpha_2$ must be satisfied [56].

- **Step 4-Sliding:** The overall stretch was selected as the sliding variable

$$\Xi_s = \lambda = \sqrt{I_4} \quad (53)$$

To describe the sliding rule for the one-dimensional fiber intrinsic hyperelasticity relation (example 2) (Eq. (51)), the form represented in Eq. (38) was employed with the sliding function as

²<https://github.com/BabakNSafa/ReactiveBond>

$$f_s(\Xi_s) = c (\Xi_s - (r_0)_s)^b \quad (54)$$

where the constant parameters $[c, b]$ are dimensionless positive numbers, and $(r_0)_s$ is the initial sliding threshold. Also, $\mathbf{e}_3$ was taken as the sliding direction and was used to define structural direction tensor as $\mathbf{M} := \mathbf{e}_3 \otimes \mathbf{e}_3$ (Eq. (38)). In this case, as long as $\lambda_s^{N-1} < \lambda_s^N < \lambda$ the condition of second law is satisfied, and it can be verified that $(-\partial \psi_{\text{EF}}(\lambda/\lambda_s^N)/\partial \lambda_s^N)(\lambda_s^N - \lambda_s^{N-1}) > 0$, which proves the compatibility of these constitutive relations with the second law (for details see the Supplementary document which is available under the “Supplemental Data” tab for this paper on the ASME digital collection). For the three-dimensional constitutive relation cases, it was assumed that Π_s^N takes the form of $\hat{F}(\lambda_s^N)$ during sliding, where by using the Taylor series expansion, it can be shown that all of the constitutive equations are compatible with the second law of thermodynamics (Supplementary document which is available under the “Supplemental Data” tab for this paper on the ASME digital collection).

- **Step 5-Damage:** For the case with damage of bonds, similar to sliding, the overall stretch was used as the damage variable

$$\Xi_D = \sqrt{I_4} \quad (55)$$

and a Weibull’s cumulative distribution function was used as the damage function [38]

$$f_D(\Xi_D) = 1 - \exp \left[- \left(\frac{\Xi_D - (r_0)_D}{l - 1} \right)^k \right] \quad (56)$$

where k is the shape parameter, l is the scale parameter, and $(r_0)_D$ is the initial damage threshold.

3.1 Sensitivity of the Formative Bonds to the Kinetics Rate

(Example 1). As discussed in Sec. 2, the kinetics rate is the predominant difference between various bond types. To show this, we simulated the response of formative bonds to a Heaviside step deformation at a wide range of reaction kinetics rate, where the only variable was the time constant (τ_f) (Fig. 5). For a large τ_f (slow kinetics rate), the response approaches the hyperelastic behavior (permanent bonds), and as τ_f gets smaller (high kinetics rate), the response approaches a singular stress behavior (sliding bonds). For all of the kinetics rates, the response at $t=0$ is the same and equal to the hyperelastic stress for that deformation. This response at $t=0$ also corresponds to the peak stress response of the initial generation in Eqs. (23) and (24).

This simple example lies at the heart of reactive inelasticity and demonstrates the consistency of inelastic behaviors that are all based on the kinetics of breaking and reforming bonds. In what

Fig. 6 Example 2: cyclic loading and damage (a) an increasing cyclic loading protocol applied for non-damaged (b) formative, (c) permanent, and (d) sliding bonds. When damage is added to the response for (e) formative, (f) permanent, and (g) sliding bonds, all the bond types show a softening behavior. The evolution of sliding and damage thresholds is also shown in (a) in response to loading and unloading phases, where sliding starts after $\lambda = (r_0)_s = 1.01$, and damage after $\lambda = (r_0)_D = 1.03$.

follows, more complex loading scenarios are investigated that are all based on a summation of incremental step deformations.

3.2 Cyclic Loading and Damage (Example 2). Example 2 demonstrates the response of single bond types with the model parameters listed in Table 2 to a cyclic loading (Fig. 6(a)). In response, formative bonds dissipate energy in a cyclic hysteresis (Fig. 6(b)), while the permanent bonds have a hyperelastic response that is independent of history of deformation (Fig. 6(c)). The sliding bonds undergo plastic deformation that is evident by the shift in the point of zero stress after each cycle, while there is no change in stiffness during the consecutive loading parts (Fig. 6(d)). Note that the sliding bonds account for strain softening that results in a decrease in stress after reaching the peak stress (points 3 and 4 in Fig. 6(d)), and it is different from strain hardening that is associated with plasticity in metals and some engineering polymers. Further, by adding damage (decreasing the total number of bonds), the Mullin's effect was captured for all three types of bonds. In addition to decreasing stiffness and the corresponding stress values, the damage increases the difference between the loading and unloading parts of the stress response. This results in increased hysteresis and further dissipation of energy (Figs. 6(e)–6(g)).

The expansion of sliding and damage thresholds is shown in Fig. 6(a) by the dashed lines. It is evident from the simulations that the behavior of bonds, especially permanent bonds with damage and sliding bonds are similar. However, certain characteristics are unique to each bond type. For example, contrary to sliding bonds, there is no shift in reference configuration for permanent bonds with damage.

3.3 Incremental Stress Relaxation With Softening and Anisotropy (Example 3). In example 3, a typical combination that may be used to model anisotropic response of tissue in a stress relaxation test is demonstrated that also includes softening. Softening in tissues often occurs at high deformations [57,58]. It is not possible to distinguish between damage and plastic deformation solely by loading the tissue in tension and analyzing the stress response. This is demonstrated in the example by using a combination of formative bonds and either sliding bonds or permanent bonds with damage (Fig. 7). In these examples, formative bonds account for the transient stress response in the axial direction, and sliding (or permanent bonds) produce the equilibrium part of the stress response (model parameters in Table 3). Identical behaviors are observed during ramp and relaxation loading phases (Fig. 7). However, during unloading, it is evident that the reference configuration is shifted when implementing the sliding bonds, where for permanent bonds with damage there is no shift in the zero-stress configuration.

Experimental evaluation of this shift in the reference configuration in soft tissue is often challenging due to nonlinearity in stress–strain behavior, when the initial stiffness is low and gradually increases by further deformation (toe-region effect). However, by having a theoretical framework for both of the candidate mechanical behaviors (i.e., plastic deformation and damage), it is possible to fit the models to the loading phase and make predictions about either the unloading phase or other experimental results (e.g., cyclic loading in example 2) to assess the success of the model in predicting the experimental data, and thus evaluating the contribution of each of the aforementioned inelastic behaviors to the tissue mechanics [59].

Fig. 7 Example 3: incremental stress relaxation with softening for ((a), (c)) formative and sliding bonds, and ((b), (d)) formative bonds with permanent bonds and damage. The effect of selection of either sliding bonds or permanent bonds is only observed during unloading. When the sliding bonds are used there is a shift in the reference configuration (c), which is not true for permanent bonds with damage (d).

4 Discussion and Concluding Remarks

This study provides a structurally inspired RIE framework for modeling inelasticity in tissue. It uses a thermodynamic scheme, where internal state variables and kinetics of molecular bonds are employed to capture the major inelastic behaviors of tissue. This framework consistently addresses a range of inelastic behaviors. The formative, permanent, and sliding bonds correspond to viscoelastic behavior with zero equilibrium stress, hyperelastic response, and plastic deformation, respectively. Additionally, the formulation of bond kinetics allows for the inclusion of damage by reducing the number of bonds, which introduces damage as an inelastic behavior to all of the bond types. Any combination of the bond types can be employed to model various kinds of observed inelastic behaviors, such as a combination of formative bonds and permanent bonds with damage to model a viscoelastic behavior with softening.

The reactive inelasticity framework uses ISV formulation, where it is usually assumed that the variables are “hidden”; however, despite the similar mathematical formulation, the variables used herein can be physically measured, and as suggested by Ateshian and co-workers are “observable state variables” [38,39]. Connective tissue’s matrix is mostly made of various types of collagen that are cross-linked. These cross-links are formed via several mechanisms including enzymatic lysyl oxidase-mediated and nonenzymatic glycation-induced cross-links to produce larger collagenous structures [60,61]. The mechanical properties of collagenous material are sensitive to the density, structure and properties of these cross-links [62]. Several studies support a correlation between mechanical loading and the state of molecular bonding as described below. Fourier-transform Raman spectroscopy during tendon’s incremental stress relaxation tests [63], and thoracic aortic wall’s ramp-to-failure [64] show that the protein conformation is highly dependent on mechanical loading. Additionally, when overloaded, collagen fibrils show local deformities (kinks) that contain denatured-collagen-rich regions [65,66]. In fact, the denatured collagen density is closely correlated with the reactive damage parameter [38]. Recent advancements in using collagen hybridizing peptides provided new opportunities to visualize the spatial distribution and level of disruption in these regions after mechanical overloading [67–69]. Furthermore, using in-silico molecular dynamics experiments, two potential mechanisms of molecular disruption, shear and tension dominant, were suggested and these closely resemble the sliding and damage processes modeled here with RIE [68]. However, despite these advances demonstrating a role for molecular bonds as observable state variables, more experimental work needs to be done to elucidate structural mechanisms of inelasticity in terms of molecular bonding.

The RIE framework is a generalization of the reactive viscoelasticity model [39], where an inclusive and consistent treatment of inelastic processes is provided. The reactive viscoelasticity model of Ateshian provided the essential concepts of weak and strong bonds that correspond to formative and permanent bonds, respectively. We chose the terminology of formative and permanent bonds because of their analogy to kinetics rate of bonds and their behavior. Additionally, in contrast to Ref. [39] we based our formulation on the number fraction of bonds rather than mass fraction, which emphasizes that in general, bonds are levels of energy and individual bonds do not correspond to a physical mass. Although at the first sight these parameters appear to be equivalent, due to their nondimensional nature, this noninertial bond assumption is particularly important when considering the singular accelerations arising in the case of sliding bonds. Massless bonds keep the model in the realm of admissibility in the general sense. Further, by making these generalizations we showed that the bonds are interchangeable at the extremes of kinetics rate, where the behavior of formative bonds is hyperelastic (permanent bonds) in the limit of slow kinetics rate (Fig. 5), and at high rates of bond kinetics formative bonds turn into sliding bonds that correspond to a plastic deformation (Fig. 6).

Plastic deformation has been experimentally observed in tissue at the macro- [4], micro- [57,70], and nano-scale [71]. Several phenomenological ISV modeling approaches have been taken to address these phenomena that often are focused to address specific inelastic behaviors and usually omit the relationships between different inelastic behaviors and their mechanisms [4,14,16,17,72]. In the current framework, we particularly focused on providing a consistent formulation between different inelastic behaviors and their structural relevance. It should be noted that the concept of sliding bonds is a fundamentally different concept compared to classic plasticity, and it rather should be compared to the theory of permanent set in polymer mechanics (rubber-like material) [22]. In a similar framework, for cross-linked polymers a molecular bond approach has been used to model stress relaxation and plastic necking instability [36,73]. However, in that theory, only plastic necking rather than general plastic deformation was addressed, and therefore, their formulation does not explicitly provide for the shift in unloaded configuration that is observed in tissue, such as nonrecoverable interfibrillar sliding [70]. In our model, the generation reference deformation gradient ($\mathbf{\Pi}^r$) is a state variable that is directly related to the plastic deformation and thus is an observable variable accounting for the shift in unloaded configuration of the material.

Damage was applied to each of the bond types regardless of their kinetics rate. This allowed for modeling the effect of damage on different components of structure that produce the mechanical behavior of material, such as degradation in the viscous components of a viscoelastic behavior without affecting its elastic part. Previously, a similar concept was used to study damage in cartilage that was only applied to the permanent bonds. This resulted in the damage effect being limited to the equilibrium behavior [38]. The reduction in number fraction of active bonds results in a decrease in the ability of material to absorb energy, which provides a generalized definition of damage as a behavior. By adding this ability, it is possible to model mechanical behavior up to rupture, where, if the formative bonds could not be damaged, no rupture could occur. Another benefit of this definition is in that it forms a clear theoretical basis for distinction between plastic deformation and damage. As shown in Fig. 6, plastic deformation alone does not result in a decrease in stiffness; however, adding damage would cause a reduction in stiffness, which is a common mechanical parameter used to assess the extent of damage in a material. By using the current theoretical framework for addressing damage and other forms of inelastic response that was provided in this study, it is possible to elucidate the mechanisms and role of each inelastic behavior in the mechanical response of tissue from the experimental stress response of the material. One future direction, for example, is using a specific loading profile with repeated scenarios (e.g., loading, unloading and reloading) to curve fit different versions of reactive inelasticity and using the fit parameters to predict an independent experimental mechanical behavior. From the quality of the predictions, one can assess the relevance of the involved inelastic behaviors and their contribution.

In this framework, one of the limitations may be that we made a continuum body assumption to relate the molecular energy to the macroscale mechanical behavior, where hierarchical structural effects, as well as statistical considerations for molecular bonding, were not included; however, the simplicity of the model and its ability to reproduce a spectrum of macroscale behaviors were chosen here over complexity of formulation. Additionally, damage was modeled as a scalar variable that may overly constrain a generalized three-dimensional case [74]. These issues can be addressed by utilizing multiple bond types with different directional preferences to achieve a desired level of anisotropy [38]. The current formulation does not study the geometry effects, spatial variation of material properties, and or other heterogeneities, which can be incorporated when RIE is solved on a certain geometry. Finally, since tissues have a significant fluid content, the fluid pressurization and poroelastic effects can play an important role in the mechanical response. Those effects were not included in

this model, which may limit applications of this framework to some experimental data. However, including poroelasticity with other material models has been studied in depth by others, thus we did not focus on that; where, a multiphasic mixture model can be used with inelastic solid phase to address fluid flow effects [2,75,76].

In conclusion, we have provided a structurally inspired framework for modeling inelastic behaviors of tissue based on the kinetics of reactive molecular bonds that break and reform in response to mechanical loading. The model addresses viscoelasticity, plastic deformation, and damage of a fibrous structure in an inclusive framework. We introduced three types of molecular bonds: formative, permanent, and sliding that result in viscoelastic, hyperelastic, and plastic deformation behaviors. Damage was applied to each of the bond types by reducing the number fraction of bonds, which consequently decreases the ability of material to absorb energy. All of the aforementioned inelastic behaviors are modeled within the same framework and by using similar sets of constitutive equations. This allows for investigating the mechanisms of inelasticity by providing a comprehensive theoretical basis for analyzing the mechanical response of tissue that can be used to understand mechanical loading induced pathological conditions, to develop more effective treatment protocols, and to engineer replacement tissues.

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Appendix: Model Parameters Used in the Illustrative Examples

The illustrative examples were designed using the noted constitutive relations to demonstrate the important features of the framework with no particular focus on certain tissues; however, in practice, specific constitutive relations should be employed to use the framework for successfully modeling of the inelastic behaviors of tissue. The models generated with this framework may have different number of model parameters. Thus, in general, no specific number of parameters could be associated with the framework. In the following, we have listed the model parameters used for different examples.

Note that the Holmes–Mow model parameters are related to the more familiar infinitesimal linear-elastic parameters as

$$\alpha_1 = \frac{E/\alpha_0}{4(1+\nu)} - \alpha_2, \quad \text{and} \quad \alpha_2 = \frac{(E/\alpha_0)\nu}{4(1+\nu)(1-2\nu)} \quad (\text{A1})$$

where E is the Young's modulus, and ν is the Poisson's ratio. Hence, $[E, \nu]$ were preferred instead of the original Holmes–Mow parameters.

Table 2 Parameters used for dynamic response of single bond types (Fig. 6)

	τ	C_2	C_3	C	b	$(r_0)_s$	k	l	$(r_0)_D$
Formative	10	0.1	40	—	—	—	—	—	—
Permanent	10^{10}	0.1	40	—	—	—	2	1.04	1.03
Sliding	0.01	0.1	40	9	2	1.01	—	—	—

Table 3 Parameters used for the incremental stress relaxation response tests (Fig. 7)

	τ	C_2	C_3	E	ν	α_0	c	B	$(r_0)_s$	k	l	$(r_0)_D$
Formative	10	0.1	40	—	—	—	—	—	—	—	—	—
Permanent	10^{10}	—	—	50	0.3	0.1	—	—	—	2	1.05	1.02
Sliding	0.01	—	—	50	0.3	0.1	8	2	1.02	—	—	—

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