Nonlocal Effect on Stiffness Measurements of a Collagen Molecule

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Accurate modeling of collagen molecules including their stiffness is essential for our understanding of mechanics of collagen fibers and tissues where these fibers play a prominent role. Studies of mechanical properties of collagen molecules employing various experimental methods and molecular dynamics (MD) simulations yield a broad range of values of the modulus of elasticity. The effect of nonlocal elasticity on the molecule stiffness derived from experiments and simulations is assessed in this brief. The estimate of the correction accounting for the nonlocal effect utilizes the exact solution of the nonlocal elasticity theory for one-dimensional elastic bars. It is demonstrated that the effect of nonlocal elasticity on the stiffness of collagen molecules can be neglected. [DOI: 10.1115/1.4029607]

Introduction

Collagen molecules are the building block of collagen fibers that are critical elements of biological tissues, including cartilage, bone, tendon, and teeth [1,2]. The hierarchy of collagen fibers and the place of collagen molecules within this hierarchy are well understood [3]. Three left-handed helical polypeptide alpha chains consisting of amino acids are combined into right-handed triple helical tropocollagen (collagen type 1) molecules. The stability of the molecule is enhanced by hydrogen bonds among and within the alpha chains [4]. These molecules are between 280 and 300 nm long and have a 1.5 nm diameter. In turn, collagen molecules arranged in a staggered pattern form fibrils that are combined in collagen fibers. Individual collagen molecules as well as fibrils formed of these molecules exhibit viscoelastic properties that were observed and investigated [1,5,6]. As shown in Ref. [7], a single molecule is adequately represented by the Kelvin–Voigt model consisting of an elastic spring and a dashpot working in parallel.

Elastic properties of a collagen molecule were estimated experimentally employing Brillouin scattering [8,9], persistence length measurements [10], X-ray diffraction [5], and optical tweezer-interferometry [11]. MD simulations have also been conducted [1,7,12]. The values of the tensile modulus found in these studies varied in a broad range from 0.35 GPa to 12 GPa. The average value recommended in Ref. [7] was 5.4 GPa. The force-elongation and engineering stress–strain relationships of collagen molecules exhibit hardening nonlinearity (e.g., Refs. [11] and [12]). Numerical MD simulations demonstrated that while the tangent modulus of elasticity of collagen molecules linearly increases with the applied tensile force (e.g., the increase is from 6 GPa to 16 GPa as the tensile force increased from zero to 3000 pN in solvated conditions), viscosity linearly decreases with tension [7]. Due to the nonlinearity of the force-elongation and stress–strain relationships, the values of the modulus of elasticity reported in literature and based on experiments and simulations refer to secant or tangent moduli.

Elastic moduli reported based on experiments or MD simulations reflect the actual properties of the molecule affected by

physical phenomena that are not always accounted for in the method employed to interpret data. In particular, nonlocal elasticity may affect the response of structures at various scale levels.

Nonlocal elasticity originated in the 1960s [13] reflecting the concept that the constitutive relationships should account for the strain tensor in the entire domain surrounding the point in question, rather than a local strain tensor at the point. A popular nonlocal model subdivides the entire material domain into the phases affected and unaffected by nonlocal effects, the latter phase being treated using the classical elastic theory [13–15]. This model was applied in Ref. [16] to develop a closed-form solution for a bar subject to tension.

The nonlocal effect may potentially be essential in collagen molecules where the external scales, such as the dimensions, may be comparable with the internal length scale accounting for the peculiarities of the microstructure. Physically, the internal length scale reflects the capacity of the material to transmit the effect of phenomena occurring at a large distance to the locations in question. The nonlocal effect has been shown significant in nanotubes [17]. Accordingly, the applicability of the classical elasticity in other nanoscale natural or engineering structures, including collagen molecules, may be questioned. This brief is concerned with the effect of nonlocal elasticity on the accuracy of the experimentally or numerically determined elastic modulus of collagen molecules.

Analysis

The secant and tangent moduli determined according to the classic elasticity theory are

$$E_{cl}^s(\bar{\sigma}) = \frac{\bar{\sigma}}{\varepsilon_{cl}}, \quad E_{cl}^T(\bar{\sigma}) = \left(\frac{d\sigma}{d\varepsilon_{cl}} \right)_{\sigma=\bar{\sigma}} \quad (1)$$

respectively, where ε_{cl} is the strain and $\bar{\sigma}$ is the applied stress. The classical theory of elasticity strain is determined directly from the inverse of the first equation (1) and from $\varepsilon_{cl} = \int_0^{\bar{\sigma}} d\sigma / E_{cl}^T(\sigma)$ using the secant and tangent moduli, respectively.

The modulus of elasticity of the molecule determined from experiments or simulations would account for the nonlocal effect if data used to evaluate the modulus was processed employing the nonlocal elasticity theory. Then the secant (E_{nl}^s) and tangent (E_{nl}^T) moduli could be referred to the nonlocal stress–strain curve and the strain replaced with the average nonlocal strain given by

$$\bar{\varepsilon}_{nl} = \frac{1}{L} \int_0^L \varepsilon_{nl}(x) dx \quad (2)$$

where L is the length of the molecule, x is the axial coordinate, and $\varepsilon_{nl}(x)$ is the nonlocal strain that varies along the molecule, contrary to the classic theory. The secant or tangent moduli of elasticity in the classic theory are related to the moduli obtained accounting for the nonlocal effect at the same applied engineering stress by

$$E_{cl}^s(\bar{\sigma}) = E_{nl}^s(\bar{\sigma}) \frac{\bar{\varepsilon}_{nl}}{\varepsilon_{cl}} = E_{nl}^s(\bar{\sigma}) \eta_1, \quad E_{cl}^T(\bar{\sigma}) = E_{nl}^T(\bar{\sigma}) \frac{d\bar{\varepsilon}_{nl}}{d\varepsilon_{cl}} = E_{nl}^T(\bar{\sigma}) \eta_2 \quad (3)$$

where η_i , ($i = 1, 2$) are correction factors for nonlocal elasticity.

The nonuniformity of the strain distribution along the molecule due to the nonlocal effect can be estimated through the strain concentration coefficient

$$k = \frac{\max[\varepsilon_{nl}(x)]}{\varepsilon_{cl}} \quad (4)$$

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A one-dimensional nonlocal formulation yields the following constitutive equation [16] that is modified here to account for the effect of stress on the secant elastic modulus:

$$\sigma(x) = E_{cl}^s(\bar{\sigma}) \left[\xi_1 \varepsilon_{nl}(x) + \xi_2 \int_0^L K(x, x') \varepsilon_{nl}(x') dx \right] \quad (5)$$

where the scalar “attenuation” function $K(x, x')$ introduces the nonlocal effect ($x \neq x'$).

The extent of dominance of classical and nonlocal theories is specified through the positive coefficients ξ_1 and ξ_2 ($\xi_1 + \xi_2 = 1$) that represent volume fractions of the material unaffected and affected by nonlocal effect, respectively. The classic theory of elasticity can be recovered if $\xi_1 = 1$, $\xi_2 = 0$.

In the incremental formulation, using the tangent modulus, Eq. (5) can be modified

$$d\sigma(x) = E_{cl}^T(\bar{\sigma}) \left[\xi_1 d\varepsilon_{nl}(x) + \xi_2 \int_0^L K(x, x') d\varepsilon_{nl}(x') dx \right] \quad (6)$$

It is tacitly assumed here that the stress magnitude does not change the volume fraction of the material affected by nonlocal effect. This is based on the assumption that the internal length, and accordingly the attenuation function adopted in the analysis [16], remains unaffected by stretching. A justification of this assumption is provided by the simulations [7] where hydrogen bonds within a collagen molecule did not change with tensile loading.

Observing that the axial stress and its increment remain constant throughout the length of the molecule Eqs. (5) and (6) can be inverted yielding

$$\varepsilon_{nl}(x) = \frac{\varepsilon_{cl}}{\xi_1} - \frac{\xi_2}{\xi_1} \int_0^L K(x, x') \varepsilon_{nl}(x') dx \quad (7)$$

and

$$d\varepsilon_{nl}(x) = \frac{d\varepsilon_{cl}}{\xi_1} - \frac{\xi_2}{\xi_1} \int_0^L K(x, x') d\varepsilon_{nl}(x') dx \quad (8)$$

respectively. The corrections factors for the secant and tangent moduli are easily obtained from Eqs. (3), (7), and (8).

Following the approach in Ref. [16], adopting the exponential shape of the attenuation function introduced by Eringen [14] and replacing Eq. (7) or (8) with two Volterra integral equations of second kind the solutions are obtained in a closed form

$$\begin{aligned} \varepsilon_{nl}(x) &= f(x, l, \lambda) \varepsilon_{cl}, \quad d\varepsilon_{nl}(x) = f(x, l, \lambda) d\varepsilon_{cl} \\ f(x, l, \lambda) &= 1 - \frac{\lambda l}{2} \left[e^{(\lambda-1/l)x} + e^{-(\lambda-1/l)x + (\lambda-1/l)L} \right] \end{aligned} \quad (9)$$

where l is the internal length scale and $\lambda = -(1 - \xi_1)/2l\xi_1$.

The correction factors for nonlocal elasticity are identical for the secant and tangent moduli

$$\eta = \eta_1 = \eta_2 = 1 - \frac{\lambda l}{L(\lambda - 1/l)} \left(e^{(\lambda-1/l)L} - 1 \right) \quad (10a)$$

For realistic combinations of internal length scale, molecule length and volume fraction of the molecule affected by the nonlocal effect, the exponential term in the right side of Eq. (10a) is negligible compared to unity yielding a particularly simple expression for the correction factor

$$\eta = 1 + \frac{\lambda l}{\lambda L - L/l} \quad (10b)$$

In the nonlocal elasticity solution for bars subjected to tension the strain concentration occurs at the ends of the bars. This is not necessarily the case in the collagen molecule loaded as a part of the fibril where the location of cross-links and bonds is unclear. However, it is still instructive to consider an idealized case where the strains are symmetric about the middle of the molecule reaching maximum values at the ends. This situation occurs if protein cross-links are attached to the end cross sections of the molecule transferring the major share of the load. The “idealized” strain concentration factor that follows from Eqs. (9) is

$$k = 1 - \frac{\lambda l}{2} \left(e^{(\lambda-1/l)L} + 1 \right) \quad (11a)$$

Neglecting the exponential term in the right side compared to unity yields an even simpler result

$$k = 1 - \frac{\lambda l}{2} \quad (11b)$$

The results given by Eqs. (10) and (11) depend on the internal length scale l and the volume fraction of the molecule unaffected by the nonlocal effect ξ_1 . As indicated in Ref. [16], values of $l \geq 0.1L$ are physically meaningless. Large volume fractions ξ_1 would indicate a virtual absence of the nonlocal effect. Using $l = 0.1L$, $\xi_1 = 0.1$ the correction factor is $\eta = 1.0818$ implying the error in the modulus of elasticity evaluated without accounting for the nonlocal effect of about 8%, while with $\xi_1 = 0.5$ this factor becomes $\eta = 1.0333$, i.e., the error is 3%. This reduction in the correction factor in the case where a larger volume fraction of the molecule is unaffected by nonlocal elasticity is anticipated. The idealized strain concentration coefficients corresponding to the two cases above are $k = 3.25$ and $k = 1.25$, respectively. Decreasing the internal length scale causes an even smaller correction; e.g., using $l = 0.01L$, $\xi_1 = 0.1$ yields $\eta = 1.0082$, i.e., the error is less than 1% (the strain concentration coefficient is $k = 3.25$). These results imply that the nonlocal effect can affect the accuracy of the modulus of elasticity obtained from experiments or MD simulations using the classic elasticity theory to interpret data only by several percent. A broad spectrum of the moduli of elasticity was determined in experimental studies and in MD simulations varying by an order of magnitude from 0.35 GPa [11] to 9 GPa [8] and 12 GPa [11]. Such variations are due to a variety of possible reasons, such as heterogeneities within the material and testing setup and procedure. Therefore, it is concluded that accounting for nonlocal elasticity of collagen molecules evaluating their stiffness is not necessary.

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