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Molecular architecture of collagen fibrils: A critical length scale for tough fibrils

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Abstract

Protein materials constitute Nature's most intriguing material concepts, leading to multi-functional and stimuli responsive materials. Such materials often feature a characteristic hierarchical design, which is characterized by structural features starting at nanoscale. Here we review recent studies of deformation of collagen, Nature's most abundant structural protein material forming the basis of bone, tendon and skin. We have discovered that a specific nanostructural design with molecular lengths of 200 nm leads to the strongest possible ultra-structure that is still capable of dissipating large amounts of energy before fracture occurs, maximizing the toughness of the material [M.J. Buehler, Proceedings of the National Academy of Sciences USA 103 (2006) 12285]. The analysis explains prevalent molecular length scales observed in tendon, bone and the eye's cornea, and explains how molecular properties influence the deformation and fracture mechanics of tissues.
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1. Introduction

Evolution in Nature has yielded a vast array of biological materials that are involved in critical functions of life. Bone, providing structure to our body, or spider silk, used for prey procurement, are examples of fascinating materials that have incredible elasticity and strength, mainly attributed to its structural formation that requires molecular precision. Many of Nature's structural materials are lightweight, but strong, elastic and tough, yet they are produced environmentally friendly with great efficiency, at moderate temperatures and at low energy cost, and are capable of dynamically adapting to changes in the environment. Despite the significance of large deformation and fracture, quantitative studies, predictive models and theories do not exist as of today.

Here we focus on collagen, the building block of tendon, bone or the eye's cornea [1–4]. Collagen, the most abundant protein on earth, is a fibrous structural protein with superior mechanical properties [2,5–12]. It consists of tropocollagen (TC) molecules with lengths of $L \approx 300$ nm with approximately 1.5 nm in diameter [2,5–7,13,14]. Staggered arrays of TC molecules form fibrils that assemble into collagen fibers (see Fig. 1). This assembly of molecules at specific length scales is highly conserved across species. This paper represents a review of earlier work by the author [16].

2. Nanomechanics of collagen during deformation and fracture

Here we review results of theoretical analyses and large-scale molecular modeling using a fully atomistic-informed, parameter free hierarchical multi-scale model of collagen fibrils (for details, see [15–18]). Due to space limitations in this paper, we cannot provide all details of these studies,

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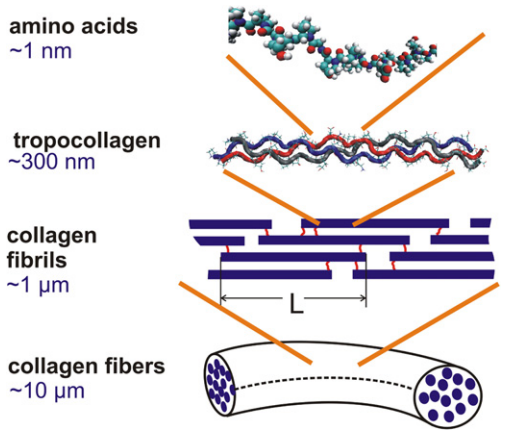

Fig. 1. Geometry of a collagen fibril, showing the characteristic hierarchical design of polypeptides, triple helical tropocollagen molecules, collagen fibrils as staggered array of tropocollagen molecules, and collagen fibers. The studies reported here are focused on the fibril scale, based on a hierarchical multi-scale model [15,16].

and we therefore refer the reader to the cited publications [15–18].

We consider single collagen fibrils under tensile loading (see Fig. 2, inlay), monitoring the stress–strain behavior as the material undergoes deformation. From the stress–strain curve, we extract the yield stress σ_{yield}, which is defined as the stress at which permanent deformation in the collagen fibril sets in. We particularly focus on the effect of the molecular length L on the deformation behavior.

2.1. Yield stress for varying molecular lengths

Fig. 2 plots the yield stress as a function of the length L of TC molecules for a cross-link free collagen fibril. For shorter molecules ($L < 200$ nm, regime I), the strength increases with L. However, the strength saturates when $L > 200$ nm (regime II). Making molecules longer than a critical length of ≈200 nm does not provide any increase in strength.

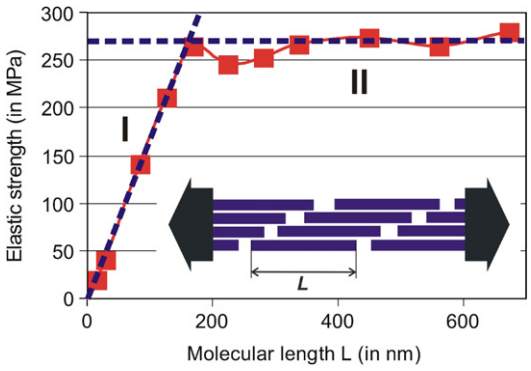

Fig. 2. Yield strength of a collagen fibril, for varying molecular lengths L (inlay shows the loading case), as obtained from molecular modeling (see Ref. [16] for details). The molecular model is derived solely from atomistic simulations, and explicitly treats the TC molecules and their interaction in the fibril. The results show a strong dependence of the strength on the molecular length L. For small values of L the strength increases (see Eq. (1)), but saturates at approximately 200 nm. The saturation is due to a change in molecular deformation mechanism. Whereas deformation is characterized by homogeneous shear for $L < 200$ nm (regime I), yield is characterized by a localized slip similar to dislocations (regime II). That is, for $L > 200$ nm, only part of the intermolecular adhesion contributes to the strength of the fibril, and therefore the strength does not increase with the molecular length, as can be verified in Eq. (2).

This behavior can be understood based on a nanomechanical analysis of the deformation mode of collagen fibrils [15,16].

2.2. Theoretical analysis

Considering a simple assembly of two parallel TC molecules (Fig. 3a), and assuming application of a homogeneous shear force along the axial direction, the tensile strength is

$$F_{\text{tens}} = \tau_{\text{shear}} L_C = \alpha \tau_{\text{shear}} L, \tag{1}$$

where L_C is the contact length, F_{tens} is the applied force in the axial molecular direction, and τ_{shear} is the shear strength of intermolecular interaction (shear force per unit length). The parameter $\alpha = L_C/L$. Due to the staggered geometry, the shear resistance increases linearly with L, thus $F_{\text{tens}} \sim \tau_{\text{shear}} L$.

However, this strength increase is only valid for short molecules, until localization of deformation takes over, when only a part of the molecule actually contributes to the strength of the material. An alternative to homoge-

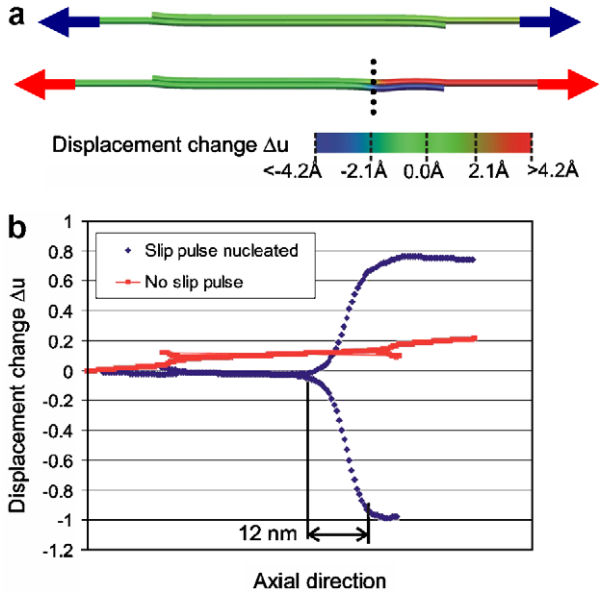

Fig. 3. Localization of intermolecular slip. The molecules are colored according to the displacements relative to an un-deformed reference configuration (displacements given in Angstroms) [16]. Subplot (a) shows the displacement fields before and after nucleation of the slip pulse (only visible in color, but subplot (b) shows identical information). One can clearly see that the displacement field changes abruptly at the location of the slip pulse. Subplot (b) shows a graph of the displacement field, along the molecule axial direction. The displacements Δu are normalized by 8.3 Å. The slip pulse is spread out over a region of approximately 12 nm. Note that the positive displacements correspond to the upper molecule, while the negative displacements correspond to the lower molecule.

neous shear is propagation of slip pulses due to localized breaking of intermolecular "bonds". In the spirit of Griffith's energy argument, it can be shown (see [15] for details) that the intermolecular slip occurs at the applied tensile force

$$F_R = \sqrt{2E\gamma} \cdot A_{\mathrm{M}}, \tag{2}$$

where E is Young's modulus of an individual TC molecule, A_{M} is the molecular cross-section and γ is the energy required to nucleate a slip pulse [16].

When $F_{\mathrm{tens}} < F_R$, deformation is controlled by homogeneous shear between TC molecules. However, when $F_{\mathrm{tens}} \geqslant F_R$ intermolecular slip pulses are nucleated. This leads to a critical molecular length

$$\chi_S = \frac{\sqrt{2\gamma E}}{\tau_{\mathrm{shear}}\alpha} \cdot A_{\mathrm{M}}. \tag{3}$$

For fibrils in which $L < \chi_S$, the predominant deformation mode is homogeneous shear and the strength depends on L (regime I in Fig. 2). When $L > \chi_S$, localized slip dominates and the strength of the fibril is independent of (regime II in Fig. 2). Comparison with Fig. 2 indicates that $\chi_S \approx 200$ nm [16]. The length scale χ_S depends on the material parameters and interaction between molecules. If γ assume very large values – for instance due to high cross-linking density, the tensile forces in each TC molecule can exceed the tensile strength of TC molecules, denoted by F_{max}, before either homogeneous shear or slip pulses are nucleated (F_{max} is a material constant that depends on the molecular structure). Thus, considering $F_{\mathrm{tens}} = F_{\mathrm{max}}$ leads to a second critical molecular length,

$$\chi_R = \frac{F_{\mathrm{max}}}{\tau_{\mathrm{shear}}\alpha}. \tag{4}$$

The length χ_R characterizes when the transition from molecular shear to brittle-like rupture of individual TC molecules occurs. The integrity of a complete collagen fibril is controlled by the strength of the weakest link, and therefore the ratio χ_S/χ_R governs the deformation mechanism: When $\chi_S/\chi_R < 1$, slip pulse nucleation governs at large molecular lengths, whereas when $\chi_S/\chi_R \geqslant 1$, fracture of individual TC molecules occurs. In both cases, the maximum strength of the fibril is reached at $L \approx L_\chi = \min(\chi_R, \chi_S)$.

Fig. 3 depicts the molecular details of nucleation of the localized slip pulse, by displaying the displacement field before and after nucleation of this defect. It can clearly be seen that the slip pulse corresponds to a highly localized region of displacement. Fig. 3a depicts the color field, and Fig. 3b depicts the displacements in a graph. Localization of the shear displacement leads to a reduced resistance of the structure against failure. Moreover, since nucleation of the slip pulse is independent of the molecular length L, the strength does not increase by changing the geometry.

The strength can only increase if the intermolecular adhesion – the prime factor that controls the critical force against slip pulse nucleation – is increased, for instance by adding covalent cross-links at the ends of the molecule.

3. Discussion and conclusion

Our analysis shows that molecular features control the nanomechanical properties of collagenous tissues. Characteristic length scales on the order of a few hundred nanometers lead to enhanced mechanical properties of collagen fibrils in order to create a tough material: A critical molecular length of ≈200 nm maximizes the toughness of collagen fibrils – making it strong, yet dissipative under large deformation (see Fig. 2).

Toughness is essential for biological function of collagen fibrils, and our findings corroborate the notion that collagen is used as a toughening material in bone, skin and other biological tissues.

Notably, collagen found in Nature typically has molecular lengths between 200 and 400 nm, in close proximity of our optimal molecular length (Fig. 2). Our analysis suggests that this particular molecular architecture has evolved and remains in so many species since it provides optimal and robust resistance to shear deformation. Similar analyses of the deformation and fracture behavior have been carried out for other protein materials, as for instance reported in [19] for alpha-helices and beta-sheets.

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