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Research paper

Nanomechanics of collagen fibrils under varying cross-link densities: Atomistic and continuum studies

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ABSTRACT

Collagen is a protein material with intriguing mechanical properties — it is highly elastic, shows large fracture strength and plays a crucial role in making Nature's structural materials tough. Collagen based tissues consist of collagen fibrils, each of which is composed out of a staggered array of ultra-long tropocollagen molecules extending to several hundred nanometers. Albeit the macroscopic properties of collagen based tissues have been studied extensively, less is known about the nanomechanical properties of tropocollagen molecules and collagen fibrils, their elementary building blocks. In particular, the relationship between molecular properties and tissue properties remains a scarcely explored aspect of the science of collagen materials. Results of molecular multi-scale modeling of the nanomechanical properties of the large-strain deformation regime of collagen fibrils under varying cross-link densities are reported in this paper. The results confirm the significance of cross-links in collagen fibrils in improving its mechanical strength. Further, it is found that cross-links influence the nature of its large-deformation and fracture behavior. Cross-link deficient collagen fibrils show a highly dissipative deformation behavior with large yield regimes. Increasing cross-link densities lead to stronger fibrils that display an increasingly brittle deformation character. The simulation results are compared with recent nanomechanical experiments at the scale of tropocollagen molecules and collagen fibrils.

1. Introduction

Collagen, the most abundant protein on earth, is a fibrous structural protein with superior mechanical properties, and provides an intriguing example of a hierarchical biological nanomaterial (Bozec and Horton, 2005; Bhattacharjee and Bansal, 2005; Anderson, 2005; Sun et al., 2004; An et al., 2004; Lees, 2003; Sun et al., 2002; Hellmich and Ulm, 2002; Jager and Fratzl, 2000; Waite et al., 1998; Borel and Monboisse, 1993; Lees, 1987; Fratzl et al., 2004; Hulmes et al., 1995). Collagen consists of tropocollagen (TC) molecules that have lengths of $L \approx 300$ nm with approximately 1.5 nm in diameter, leading to an aspect ratio of close to 200 (Bozec and Horton, 2005; Bhattacharjee and Bansal, 2005; Sun et al., 2004; Hulmes et al., 1995; Puxkandl et al., 2002; Sasaki and Odajima, 1996). Staggered arrays of TC molecules form fibrils, which arrange to form collagen fibers. A schematic of the main hierarchical features of collagen is shown in Fig. 1.

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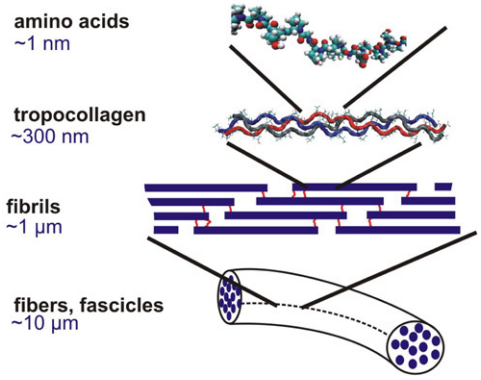

Fig. 1 – Schematic view of some of the hierarchical features of collagen, ranging from the amino acid sequence level at nanoscale up to the scale of collagen fibers with lengths on the order of 10 μm. The present study is focused on the mechanical properties of collagen fibrils, consisting of a staggered array of TC molecules. The red lines in the graph indicate intermolecular cross-links that are primarily developed at the ends of tropocollagen molecules. In this paper, particular attention is paid to the mechanical properties as a function of varying cross-link densities. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Collagen plays an important role in many biological tissues, including tendon, bone, teeth, cartilage or in the eye's cornea (Bozec and Horton, 2005; Bhattacharjee and Bansal, 2005; Hellmich and Ulm, 2002; Borel and Monboisse, 1993; Puxkandl et al., 2002; Bozec et al., 2005; Buehler, in press). Severe mechanical tensile loading of collagen is significant under many physiological conditions, such as in joints and in bone (Nalla et al., 2005; Ritchie et al., 2004).

Despite the significance of the large-deformation behavior of collagen based tissues, few studies have been reported focusing on analyzing the fundamental deformation mechanisms under mechanical load. In particular, the relation of the molecular and intermolecular properties with tissue properties are not understood well. Moreover, the limiting factors in strength of collagen fibrils, and the origins of toughness remain largely unknown. Experimental efforts focused on the deformation mechanics of collagen fibrils at nanoscale, including characterization of changes of *D*-spacing and fibril orientation (Hulmes et al., 1995; Sasaki and Odajima, 1996; Orgel et al., 1995), analyses that featured in X-ray diffraction (Hulmes et al., 1995) and synchrotron radiation experiments (Puxkandl et al., 2002). Other experimental studies were focused on the averaged response of arrays of collagen fibrils, considering nanoscale deformation mechanisms (Gupta et al., 2005).

Most research was focused on the macroscopic, overall mechanical properties of collagen fibers and scales beyond, for example of tissues, often without explicitly considering the molecular nanoscale structure (Bozec et al., 2005). Other studies focused on the properties of individual TC molecules, without linking to the macroscopic materials' response (Bhattacharjee and Bansal, 2005; Sun et al., 2004; An et al., 2004; Lorenzo and Caffarena, 2005).

There exist few models that link properties of individual molecules with the overall mechanical response of fibrils or fibers, considering the different types of chemical bonding and nanoscale mechanics and geometry. Constitutive models of the mechanical behavior of collagen fibrils typically feature empirical parameters or are derived from experimental observations. However, such models are not predictive since they are not based on fundamental molecular details of the chemical bonding in collagen.

1.1. *Predictive atomistic based modeling of deformation and fracture collagen*

In order to develop a fundamental and quantitative understanding of collagen mechanics, theoretical models encompassing the mesoscopic scales between the atomistic and the macroscopic level, considering atomistic and chemical interactions during deformation are vital. This represents an alternative strategy capable of predicting the properties of collagen tissue from the bottom up.

In order to achieve this goal, a parameter free atomistic based model of the mechanical properties of collagen fibrils, based solely on atomistic simulation input data (Buehler, 2006a,b) can be used.

1.2. *Research strategy*

To understand the influence of cross-links on the deformation mechanics of collagen fibrils, a series of computational experiments of pulling individual collagen fibrils with increasing density of cross-links is carried out. All results are compared with a control system of a cross-link free collagen fibril. Systematic increases of the density of cross-links enables one to observe the difference in mechanical behavior. Particular attention is paid to the small- and large-deformation behavior and the effect of intermolecular cross-links on the mechanical properties and deformation mechanisms.

In particular, studies are carried out that focus on the changes in the elastic and fracture behavior of the collagen fibril as the parameters are varied. An analysis of the molecular mechanisms allows one to develop a mechanistic understanding of the deformation behavior of collagen fibrils.

2. Molecular model of collagen fibrils

2.1. *Reactive mesoscopic model: Formulation*

The studies reported in this paper are carried out using a reactive mesoscopic model describing TC molecules as a collection of particles interacting according to multi-body potentials, as described in a series of earlier publications (Buehler, 2006a,b). The present paper describes an application of this molecular model, and thus details about model development are omitted.

The mesoscopic, molecular model does not contain full atomistic information about all atoms in the residues and all side chains, since it is based on the idea of representing