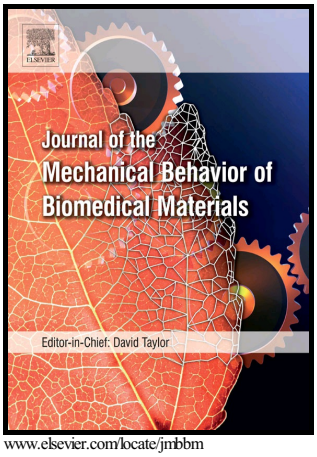
Mechanical properties of a collagen fibril under simulated degradation

David C. Malaspina, Igal Szleifer, Yasin Dhaher



www.elsevier.com/locate/jmbbm

PII: S1751-6161(17)30363-6
DOI: http://dx.doi.org/10.1016/j.jmbbm.2017.08.020
Reference: JMBBM2464

To appear in: *Journal of the Mechanical Behavior of Biomedical Materials*

Received date: 11 March 2017
Revised date: 10 August 2017
Accepted date: 15 August 2017

Cite this article as: David C. Malaspina, Igal Szleifer and Yasin Dhaher, Mechanical properties of a collagen fibril under simulated degradation, *Journal of the Mechanical Behavior of Biomedical Materials,* http://dx.doi.org/10.1016/j.jmbbm.2017.08.020

Mechanical properties of a collagen fibril under simulated degradation.

David C. Malaspina[a,b], Igal Szleifer[a], Yasin Dhaher[a,b*]

[a]Biomedical Engineering Department, Northwestern University, 2145 Sheridan Road, Evanston, IL 60208, USA.

[b]Rehabilitation Institute of Chicago, 345 E. Superior, Chicago, IL 60611, USA. Collagen, molecular dynamics, degradation, MMP

[*]**Corresponding author.**

ABSTRACT:

Collagen fibrils are a very important component in most of the connective tissue in humans. An important process associated with several physiological and pathological states is the degradation of collagen. Collagen degredation is usually mediated by enzymatic and non-enzymatic processes. In this work we use molecular dynamics simulations to study the influence of simulated degradation on the mechanical properties of the collagen fibril. We applied tensile stress to the collagen fiber at different stages of degradation. We compared the difference in the fibril mechanical prorties due the removal of enzymatic crosslink, surface degradation and volumetric degradation. As anticipaded, our results indicated that, regardles of the degreadation senario, fibril mechanical properties is reduced. The type of degradation mechanism (crosslink, surface or volumentric) expressed difrential effect on the change in the fibril stiffness. Our simulation results showed dramatic change in the fibril stiffness with a small amount of degradation. This suggests that the hierachical structure of the fibril is a key component for the toughness and is very sensitive to changes in the organization of the fibril. The overall results are intended to provide a theoretical framework for the understanding the mechanical behavior of collagen fibrils under degradation.

INTRODUCTION:

The molecular structure of collagen is characterized by a hierarchical multi-scale organization that grants high elasticity, large fracture strength and large energy dissipation upon deformation [1]. The key building block is the tropocollagen molecule formed by a triple helix of three polypeptides chains with a length of ~300 nm. Tropocollagen molecules arranged in groups to form more complex structures: micro-fibrils, fibrils and fibers. Micro-fibrils have an approximate diameter of ~4 nm and are the minimum structure that presents the characteristic D-banding as a consequence of gaps and overlaps between tropocollagen. These micro-fibrils self-assemble in larger bundles forming collagen fibrils. The approximate length of fibrils is on the order of ~1μm. Finally, bundles of fibrils form higher hierarchy units: the collagen fibers. These fibers are the main constitutive unit of different connective tissues and the approximate length is ~10 μm[2-4]. In this work we are going to focus on the intermediated hierarchy level: the collagen fibrils.

In healthy tissue, collagen production is balanced by collagen degradation. The degradation of collagen is mediated in some cases by matrix metallo-proteinases (MMPs), enzymes that bind and cleave the triple helical tropocollagen molecule. If the balance between collagen production and degradation is disrupted, many disease states emerge, including post traumatic remodeling, arthritis, cancer, and fibrosis [5-9]. Understanding the connection between collagen degradation and the associated change in mechanical properties of collagen at the tissue level may lead to the development of tissue remodeling therapies for different pathologies.

During the last decade, improvement in experimental techniques allowed for a broader understanding of the effect of collagen degradation on the basic mechanics at the tissues level [10-13]. For example, using a bovine knee articular cartilage, Laasanen and colleagues reported up to 70% reduction in the tissue's static elastic modulus after a chronic exposure to collagenase type IV (MMP) [11]. Consistent results have also been observed by Park and collaborators who reported near 60% enzyme-mediated reduction in the equilibrium elastic modulus of bovine articular cartilage [10].

At the fiber level, Panwar et al. explored the effect of degradation on the mechanical properties of tendon collagen fibers using the mice tail [12, 13]. In these examinations, a cathepsin K (a cysteine protease) was employed to degrade the collagen fibrils. A significant reduction of the elastic modulus (~ 60%) and the associated ultimate stress at rupture was observed [12]. Using data from tissue and fiber level experiments, phenomenological models have been developed to describe the aggregate effect of enzyme-mediated changes on tissues mechanics. Unfortunately, these mathematical description of degradation does not take in account the molecular complexity of collagen degradation [14-17]. While a connection between molecular structure and mechanical properties have been drawn in some experimental studies [12, 13],