MATHEMATICAL MODELLING OF TENDON MECHANICS

Franco Maceri, Michele Marino, Giuseppe Vairo
Università degli Studi di Roma "Tor Vergata", Italy

Corresponding author: Giuseppe Vairo, Department of Civil Engineering, Università degli Studi di Roma "Tor Vergata"– via del Politecnico 1 – 00133 Roma, Italy; vairo@ing.uniroma2.it

Abstract. In this paper, the mechanical response of tendons is modelled by a two-step homogenization approach, based on a multiscale model of the tissue elastic behaviour. Tendons large-strain and large-displacement elasticity is numerically studied by an iterative algorithm, involving the solution of a sequence of linearized problems. Thereby, the nanomechanics of collagen is included into the micromechanics of fibrils which finally affects the macromechanical behaviour of tendons, computed according to the theory of fiber-reinforced composite materials. Starting from very few model parameters, fully consistent with histological and morphological evidences, effectiveness and accuracy of the proposed model have been proved reproducing a tensile experimental test on a rat tail tendon.

1 Introduction

Tendon is a dense connective tissue, transmitting muscular forces to the skeleton [1], and is constituted by an organized hierarchical structure, from the molecular scale up to the macro one (see Fig. 1) [2]. As confirmed by the specialized literature [3, 4, 5, 6, 7, 8, 9], analysis and modelling of tendon mechanics at different scales represents a frontier challenge which should open to the understanding of a number of physiological processes. For instance, at the micro scale the cellular mechanics and the related strain response seems to affect strongly the molecular pathways leading to tissue remodelling, as well as at the macro scale the mechanical behaviour of joints deeply depends on tendon and ligament mechanics .

The mechanical response of tendons depends primarily on the behaviour and structure of their constituents. Tendons contain 86% collagen, 1-5% proteoglycan, and 2% elastin as measured by dry weights, and water is responsible for 60-80% of the total wet weight of the tissue [10, 11]. In tendons, collagen volume fraction has been reported to be about 50% [12].

The tropocollagen or "collagen molecule" (of type I) is a rod-shaped protein about 300 nm long and 1.5 nm in diameter; collagen fibrils are collagen molecules packed into an organized overlapping bundle, whose structure is characterised by molecular kinks [9]. Collagen fibrils are densely packed in bundles called fibers and each hierarchical level of collagen assembly is stabilized by numerous covalent cross-links between collagen molecules (see Fig. 1). The fibrils within the fibre are tilted, leading to a macroscopic crimped structure. Morphological observations suggest that collagen fibers in tendons are practically arranged in a planar wavy array and are aligned along the loading direction.

Due to this microstructure, tendon mechanical characteristics depends on the collagen fibers. Upon stretch, they become gradually straight and this process is accompanied by an increase in tissue stiffness.

Experimental tests highlight that typical tendon stress/strain curves can be subdivided into three regions (Fig. 1):

1. Toe region: the region of small strains (up to 2%) corresponds to the removal of the microscopic crimp (with a period of order of 100–300 μm) in the collagen fibrils.
2. Heel region: at strains 2% to 5%, tendon stiffness increases considerably with the tissue stretching. This response has been justified by considering molecular kinks within the collagen fibril structure at the nano scale. The straightening of the kinks induce a further elongation of the fibril..
3. Linear region: when collagen is stretched beyond the heel region, most kinks are straightened and no further extension is possible by the mechanisms described above. Therefore, the linear region is primarily affected by the stretching of the collagen triple-helices and in a negligible way by a molecular rearrangement (collagen sliding and increase in gap between molecules) [13].

Several constitutive models have been recently proposed for collagenous tissues, such as tendons, based on a continuum approach and involving a macroscopic mechanical description. Most of them are deduced from phenomenological evidences, introducing material parameters having no direct physical or morphological basis. Exponential and power-law functions are widely employed [3, 4, 5]. Other approaches take into account geometrical non-linearities by considering crimped collagen fibers comprising linearly elastic material, with sinusoidal [6, 7] or helical geometry [8]. Although these models are able to describe a non-linear stress-strain behaviour similar to the one of collagenous tissues, they lack a suitable experimental validation or they are based on model parameters obtained by parametric fitting of experimental data, ignoring any histological and morphological evidences. Moreover, they do not take into account the crucial role of the non-linear collagen constitutive behaviour, deeply related to nano-scale entropic processes and affecting heel region response [9].

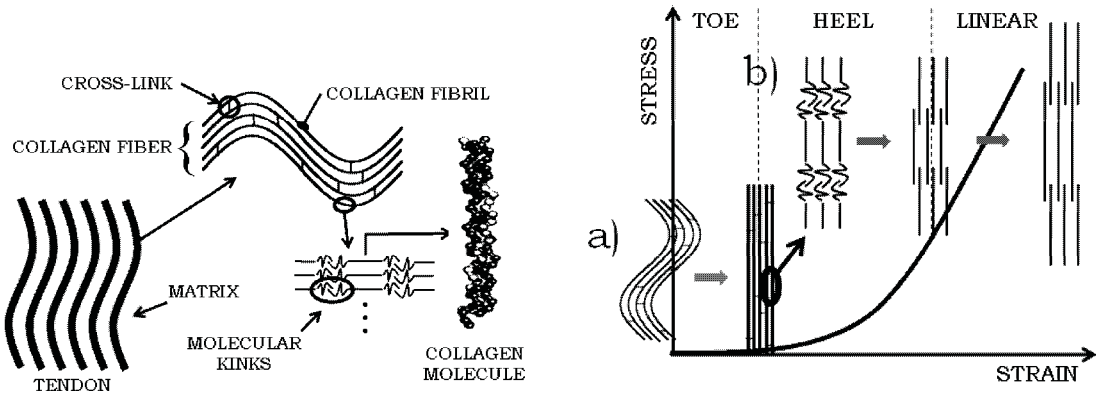

Figure 1: Left: The hierarchical structure of tendon. Right: Typical stress-strain curve for a tendon tissue. a) Microscopic crimp of the fibrils is removed; b) molecular kinks at nano scale are straightened.

The rationale which leads the present work is the evidence that tendons can be structurally regarded as a composite material with a reinforcement phase (i.e., collagen fibrils) practically aligned in the preferred loading direction. Considering linearly elastic constitutive behaviour for each phase and straight fibers, these aspects could be easily considered by classic theories of fiber reinforced composite materials [14]. Unfortunately, in biological tissues, collagen fibers are crimped and their local material response is highly non-linear. Accordingly, a more refined approach has to be developed.

In the present work, tendon mechanics is modelled by a two-step homogenization technique, based on a multiscale approach. First a micromechanical homogenization procedure is employed in order to reduce a crimped fiber to an equivalent straight one, and then a classical homogenization approach is involved to reduce the tendon tissue (constituted by equivalent straight fibers embedded into a matrix) to a one-dimensional homogeneous structure, subjected to uniaxial traction along the fiber direction. Moreover, a generalized version of the Worm-Like Chain (WLC) model [15, 16], traditionally employed in DNA so-called "entropic elasticity", is proposed in order to describe the non-linear constitutive behaviour of collagen, in agreement with nano-scale evidences [17].

Tendons large-strain and large-displacement elastic equilibrium response is numerically computed by an iterative algorithm, involving the solution of a sequence of linearized problems. Model parameters are related with measurable histological and geometrical properties and are consistent with reference values available in specialized literature. Finally, in order to show soundness and effectiveness of the model a tensile experimental test on a rat tail tendon is numerically reproduced.

2 A multiscale mechanical model

2.1 Nanomechanics of collagen

In order to describe the non-linear constitutive behaviour of collagen material, we consider the nanomechanics of collagen molecule by means of a generalized version of the Worm-Like Chain model (WLC) [15]. The WLC is a model of entropic elasticity for a macromolecule (a chain of atoms) under thermal agitation. Following Norris et al. [16], the relationship between the entropic force $\mathcal{F}$ acting on a molecule and the molecule extension z, that is its end-to-end length, can be expressed as:

$$\mathcal{F} = \frac{k_B T}{L_p}\left\{\frac{1}{4}\left(1-\frac{z}{L_c}\right)^{-2} - \frac{1}{4} + \frac{z}{L_c} - \frac{3}{4}\left(\frac{z}{L_c}\right)^2 + \frac{1}{64}\left(\frac{z}{L_c}\right)^3\left[3-5\left(\frac{z}{L_c}\right)\right]\left[19-20\left(\frac{z}{L_c}\right)\right]\right\} \qquad (1)$$

where k_B is the Boltzmann constant, T is the molecular absolute temperature, L_p is the molecular persistence length, giving a measure of alignment of the chain [16], and L_c is the chain contour length, that is the length of the outstretched macromolecule.

It is worth observing that relationship (1) exhibits a pole for $z = L_c$. Accordingly, when $z \to L_c$ the entropic force $\mathcal{F}$ tends to infinity, corresponding to a rigid molecular behaviour. Traditionally, the classical WLC model has been implemented and applied to DNA [15], where interest in molecule extensibility is focused only on small values of applied force. Nevertheless, as remarked in [17], a certain molecular degree of extensibility should be considered in proximity of the contour length L_c in order to improve the WLC accuracy for collagen molecule under high extensions.

With the aim to generalize this approach to the case of collagen extensible molecule, let σ_c and ε_c to be introduced

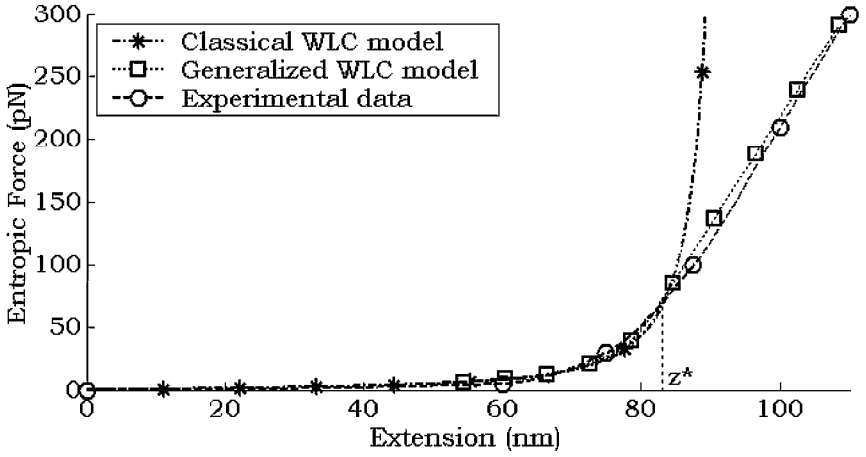

Figure 2: Force-extension curve for a single collagen monomer. Comparison between experimental data (○) [17], classical (∗) and generalized (□) WLC models. $E_{high} = 3.4$ GPa, $L_{in} = 50$ nm, $A_c = 1.76$ nm^2.

as the molecular nominal stress and strain measures, respectively:

$$\sigma_c = \mathcal{F}/A_c, \qquad \varepsilon_c = z/L_{in} - 1 \tag{2}$$

where A_c is the molecule cross-section and L_{in} is a reference molecule end-to-end length, depending on biological and chemical molecular surrounding. It is worth observing that, in agreement with experimental evidences obtained in [18], the reference end-to-end molecular length can be set as $L_{in} = L_c - l_{kinks}$, where l_{kinks} represents an average measure of the kink dimension occurring within the fibril structure (about 20 nm [18]).

Let the following one-dimensional non-linear constitutive equation of the molecule to be introduced:

$$\sigma_c(\varepsilon_c + \Delta\varepsilon_c) = \sigma_c(\varepsilon_c) + \left.\frac{\partial \sigma_c}{\partial \varepsilon_c}\right|_{\varepsilon_c} \Delta\varepsilon_c + o(\Delta\varepsilon_c) \approx \sigma_c(\varepsilon_c) + E_c(\varepsilon_c)\Delta\varepsilon_c \tag{3}$$

$E_c(\varepsilon_c)$ being the molecular tangent elastic modulus at the actual strain level ε_c. It can be regarded as a measure of tangent modulus for collagen material and is here defined as:

$$E_c(\varepsilon_c) = \begin{cases} \left.\frac{\partial \sigma_c}{\partial \varepsilon_c}\right|_{\varepsilon_c} & \text{for } z < z^* \\ E_{high} & \text{for } z \geq z^* \end{cases} \tag{4}$$

where $\frac{\partial \sigma_c}{\partial \varepsilon_c}$ is computed combining Eqs. (1) and (2), $z^* = L_{in}(\varepsilon_c^* + 1)$ is strictly less than L_c and is such that $\left.\frac{\partial \sigma_c}{\partial \varepsilon_c}\right|_{\varepsilon_c^*} = E_{high}$. The parameter E_{high} denotes the upper bound for E_c and it can be regarded as the Young's modulus of collagen under significant extension. Accordingly, it can be set within the physiological range (0.5 – 6 GPa) estimated by several authors [19, 20], depending on tissue nature, experimental procedures and strain level.

The proposed generalized WLC model has been validated by comparing the present model results with the experimental data reported in [17], where collagen force-extension behaviour is measured by atomic force microscopy and fitted into a classic WLC model (assuming $L_c = 95$ nm and $L_p = 1$ nm [17]). As shown in Fig. 2, both the generalized and the classical WLC models accurately describe the low force experimental collagen's behavior, but the former one is much more accurate for high forces, reproducing the tensile response of collagen molecule for high extension values.

2.2 Micromechanics of collagen fibrils and fibers

The mechanics of collagen fibrils is highly dependent on their initial configuration. Indeed, as firstly remarked, the presence of a crimp influences the fibril force-elongation curve inducing a significant toe region.

Moreover, it is worth observing that fibrils in all collagenous tissues are closely jointed by means of so-called "cross-links", leading to histologically units called fibers, characterizing the structural reinforcement phase for the tissue.

In this paper, in agreement with other specialized results [7, 6], the characteristic planar periodic shape of a tendinous collagen fiber is modelled considering a sinusoidal beam, with circular cross-section of radius r_f, whose reference configuration is defined by the period L_0 and the amplitude H_0.

Following the multiscale asymptotic expansion method proposed by Haussy et al. [21], the equivalent along-the-chord stiffness of the fiber is:

$$(EA)_{f,\,eq} = (E\,\langle\cos\alpha\rangle)\left[\frac{\langle\cos^2\alpha\rangle}{A} + \frac{\langle(f(x))^2\rangle}{I}\right]^{-1} \tag{5}$$

where E is the Young's modulus of the fiber material, A is the fiber cross-section, $I = \pi r_f^4/4$, $\alpha(x)$ represents the tangent slope (evaluated with respect to the chord axis, namely x) of the fiber centerline curve whose equation is $f(x)$, and symbol $\langle\cdot\rangle$ denotes the curvilinear average operator defined as:

$$\langle g\rangle = \frac{1}{\mathcal{L}}\int_0^{\mathcal{L}} g(s)ds \tag{6}$$

where $\mathcal{L}$ is the actual curve length of a period, and s is the curvilinear coordinate along the fiber centerline, such that $s \in [0,\mathcal{L}]$.

Assuming E equal to the tangent collagen modulus E_c defined by Eq. (4), the relationship (5) can be iteratively employed for describing the non-linear stress/strain behaviour of a collagen fiber, including nanomechanics effects. At each step, the molecular collagen strain ε_c is computed as the actual fiber's centerline stretch:

$$\varepsilon_c = \frac{\mathcal{L}}{\mathcal{L}_0} - 1 \tag{7}$$

$\mathcal{L}_0$ being the reference fiber's centerline length over a period. Therefore, for a given along-the-chord force increment the value of E_c is updated at the strain level ε_c and the actual equivalent fiber stiffness $(EA)_{f,\,eq}$ is computed by using the actual fiber geometrical parameters. Finally, the displacement field satisfying the incremental elastic equilibrium's problem is computed by means of principle of virtual work, leading to an updated actual fiber configuration. It is worth observing that, since during the deformation process the fiber does not remain sinusoidal, at each iteration step the function $f(x)$ occurring in Eq. (5) have to be evaluated considering discrete interval along the chord axis x.

Referring to nominal apparent (i.e., along-the-chord) fiber's stress σ_f and strain ε_f, Fig. 3 shows the typical non-linear constitutive behaviour of a collagen fiber evaluated through the proposed approach, as well as the fiber equivalent along-the-chord elastic modulus versus the nominal strain. The results are obtained considering a collagen fiber with $r_f = 0.5\ \mu$m, $L_0 = 250\ \mu$m, $H_0 = 10\ \mu$m and including or not nano-mechanics effects. It clearly appears as considering nano-scale entropic mechanisms a more gradual fiber response arises than the classical elasticity approach. Moreover, the results put in evidence as the removal of the fiber crimp (corresponding to a straight fiber configuration and to a value of the apparent strain equal to ε_f^*) can be related to negligible values of the apparent stress.

Often, available experimental data indicate average values of the fiber period L_0 and of ε_f^*. Therefore, in order to deduce a consistent measure of H_0, it can be observed that for a sinusoidal fiber the reference curve length over a period is expressed as:

$$\mathcal{L}_0 = \frac{2L_0}{\pi}\sqrt{1+\omega^2}\,\mathcal{E}\left(\frac{\omega}{\sqrt{1+\omega^2}}\right) \tag{8}$$

where $\omega = 2\pi H_0/L_0$ and $\mathcal{E}(x)$ is the elliptic integral of the second kind, defined by the following power series:

$$\mathcal{E}(x) = \frac{\pi}{2} - \frac{\pi}{8}x^2 + \ldots \tag{9}$$

Therefore, when ω tends to zero (i.e., when H_0 tends to zero), and disregarding the fiber material stretch upon to the crimp removal, the following approximated relation can be stated:

$$\mathcal{L}_0 \cong L_0\left(1+\frac{\omega^2}{4}\right) \cong L_0(1+\varepsilon_f^*) \tag{10}$$

or equivalently

$$H_0 = \frac{L_0}{\pi}\sqrt{\varepsilon_f^*} \tag{11}$$

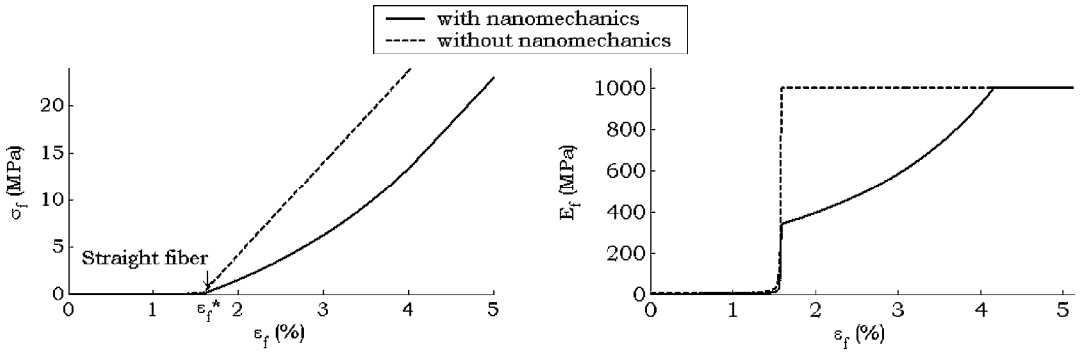

Figure 3: Nominal equivalent (along-the-chord) stress/strain behavior of a collagen fiber with $L_0 = 250$ μm, $H_0 = 10$ μm and $r_f = 0.5$ μm (on the left) and equivalent along-the-chord elastic modulus versus the nominal strain (on the right). Comparison between results obtained including nanomechanics effects ($L_c = 285$ nm [19], $L_p = 14.5$ nm [19], $l_{kinks} = 22$ nm [18], $E_{high} = 1$ GPa [20]) and without nanomechanics ($E_c = \text{const.} = 1$ GPa).

2.3 Macromechanics of tendons

Once a crimped collagenous fiber is homogenized in an equivalent straight fiber accounting for geometrical and entropic constitutive non-linearities, the macromechanics of tendons can be formulated employing the classical theory of fiber-reinforced composite materials, considering equivalent collagenous straight fibers embedded into a soft linearly elastic isotropic matrix.

In agreement with in vivo evidences, tendon can be regarded as a one-dimensional structure subjected to uniaxial traction along the fiber direction. By employing the mixture rule, the equivalent tendon axial modulus E_t can be computed as:

$$E_t(\varepsilon_t) = V_f E_f(\varepsilon_f) + (1 - V_f) E_m \tag{12}$$

where V_f is the fiber volume fraction in tendon assumed to be equal to 0.5 [12], E_m is the Young modulus of the non-collagenous matrix assumed to be equal to 1 MPa [22], E_f is computed by Eq. (5) at the fiber strain level ε_f and involving the value of E_c (see Eq. (4)) at the collagen strain level ε_c. It should be observed that, due to the considered one-dimensional approach, $\varepsilon_f = \varepsilon_t$, that is the nominal fiber strain measure is both an apparent (along the chord) microscopic strain measure for the collagenous fibers and a macroscopic one for the overall tendinous tissue (ε_t).

It should be remarked that damage effects, fiber-fiber and fiber-matrix interactions are herein neglected. Indeed, damage mechanisms are behind the scope of the present work. Fiber-fiber interaction can be disregarded because, for the sake of maximum compactness, close fibers can be assumed to have similar geometry and therefore the same straightening process. Finally, high ratios between fiber and matrix stiffness justify the fiber-matrix interaction disregarding.

Briefly, the iterative nano-micro-macro algorithm employed to describe the non-linear tensile behaviour of a tendon can be summarized as follows.

For the ith step:

1. impose a tendon strain increment $d\varepsilon_t = d\varepsilon_f$;
2. compute fiber's material (i.e. collagen) strain $\varepsilon_{c,i}$ (see Eq. (7));
3. compute the elastic modulus of the collagen at the achieved material strain $E_c(\varepsilon_{c,i})$ from Eq. (4);
4. compute the equivalent elastic modulus of the fiber $(EA)_{f,eq}$ from Eq. (5);
5. compute the macroscopic equivalent tendon modulus E_t from Eq. (12) and the actual macroscopic stress into the tendon as $\sigma_{t,i} = \sigma_{t\,i-1} + E_{t,i}\, d\varepsilon_{t,i}$;
6. update fiber geometry for successive steps with the principle of virtual work;
7. come back to point 1 with $i = i + 1$;

This nano-micro-macro algorithm has been implemented into a parametric homemade MATLAB® code.

It is worth observing that the full model here proposed can be established on the basis of very few parameters, easily determined by experiments.

3 Model validation

The numerical results obtained by present model are put in comparison with the experimental results proposed in [23], where experimental data on fiber reference configuration are also given. In detail, optical coherence tomography (OCT) images reported in [23] show an average crimp period of $L_0 = 240\ \mu m$. Moreover, it has been measured that the 50% of the fibers extinguish crimp at 2% of the tissue strain. Accordingly, assuming $\varepsilon_f^* = 2\%$, crimp amplitude is computed by Eq. (11), resulting $H_0 = 10.8\ \mu$m. Following Graham's evidences [18], kinks' length has been assumed equal to 22 nm and E_{high} is set equal to 1 GPa [20].

In order to show the effectiveness of the proposed multiscale nano-micro-macro approach, the relevant numerical results are compared in Fig. 4 with both those obtained through a micro-macro formulation (assuming $E_c =$ const. $= 1$ GPa) and experimental measures.

The micro-macro approach qualitatively reproduces the tendon mechanical response and in particular the stiffness increase at the end of the toe region and the stress/strain slope into the linear region. But micro-macro approach is absolutely unable to describe the tendon behaviour in the heel region. On the other hand, when entropic mechanisms are taken into account through the proposed nano-scale formulation, a gradual increase of tendon elastic modulus is obtained also when $\varepsilon_t > \varepsilon_f^*$), producing an excellent fit of the experimental measures on each characteristic region of the stress/strain curve.

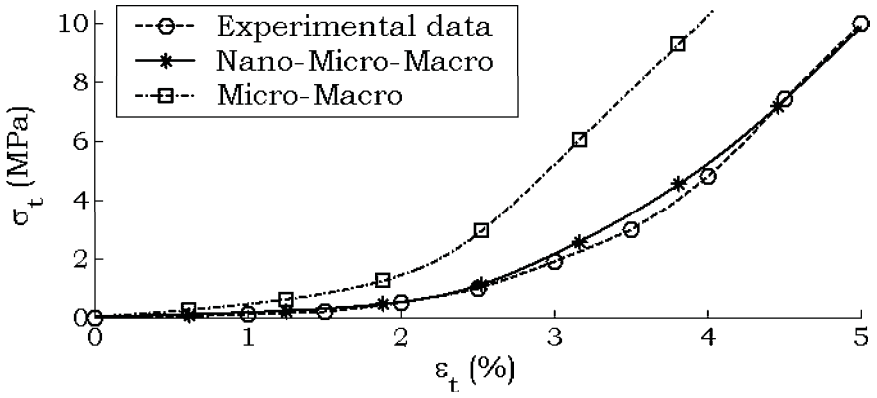

Figure 4: Experimental stress/strain response (○) for a rat tail tendon [23] compared with the numerical results obtained by the proposed model, considering both a micro-macro (□, $E_c =$ const. $= 1$ GPa [20]) and a nano-micro-macro ($*$) approach ($L_c = 285$ nm [19], $L_p = 14.5$ nm [19], $E_{high} = 1$ GPa [20], $l_{kinks} = 22$ nm [18]). $L_0 = 240\ \mu$m [23], $H_0 = 10.8\ \mu$m (from Eq. (11)), $r_f = 4\ \mu$m [24], $V_f = 0.5$ [12], $E_m = 1$ MPa [22].

4 Conclusions

In this paper, tendon mechanics has been addressed introducing a multiscale formulation of the tissue elasticity problem. In detail, a two-step homogenization technique has been adopted, in order to take into account the presence of a crimped collagen fibers embedded into an extra-cellular matrix. Moreover, the collagen constitutive non-linearities have been modelled describing the nanomechanics of collagen molecule by means of an entropic model based on a generalized version of the Worm-Like Chain model. Tendons large-strain and large-displacement elastic equilibrium solution is numerically computed by an iterative algorithm, involving the solution of a sequence of linearized problems.

The full model depends on very few mechanical or geometric parameters, experimentally measurable.

Using values for the model parameters fully consistent with histological and morphological evidences, effectiveness and accuracy of the proposed model have been proved reproducing a tensile experimental test on a rat tail tendon. Relevance of nano-scale mechanisms has been clearly highlighted, showing the excellent fit with the experimental results.

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