MINI-COURSE

Mechanical modeling of soft biological tissues

LESSON 1

The multiscale structural approach: the case of tendons

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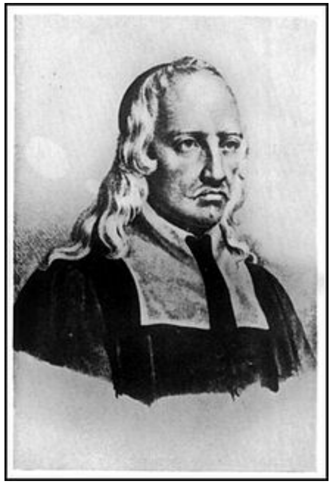
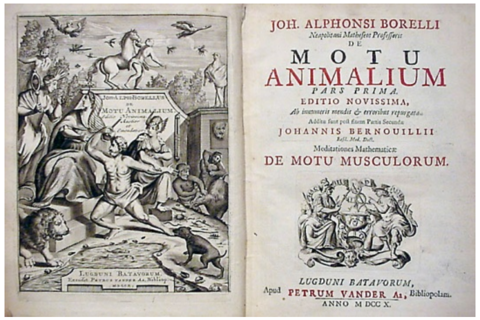
University of Rome "Tor Vergata"

Biomechanics?

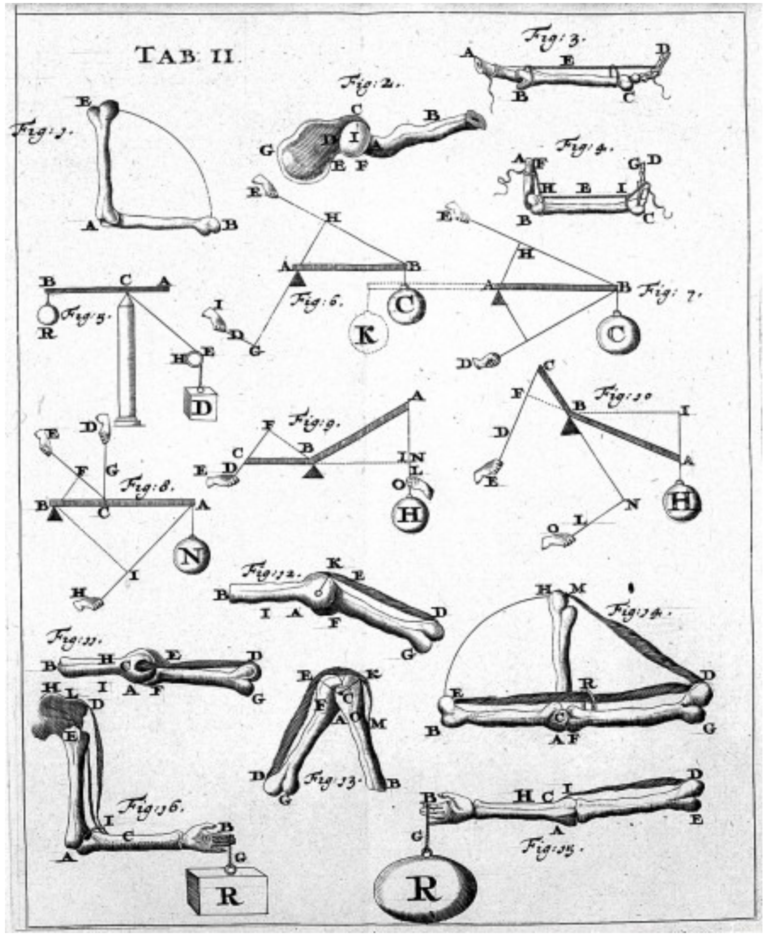
"Biomechanics is the study of the structure and function of biological systems by means of the methods of mechanics"

Herbert Hatze, University of Vienna, 1974





Giovanni Alfonso Borelli
Napoli, 1608-1679



Biomechanics? … not exclusively!

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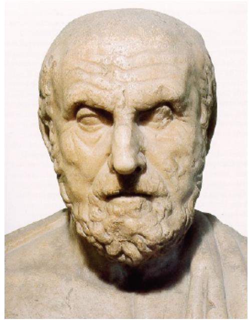
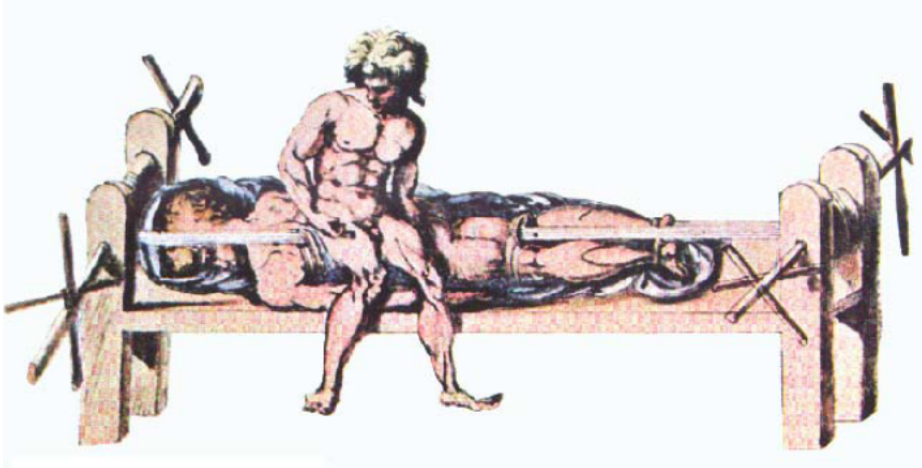
Herbert Hatze, University of Vienna, 1974



Ippocrate
460-370 a.c.

Treatment for back pain:
the patient is tied to a sort of scale and the force of gravity is exploited to relieve the pressure on intervertebral discs



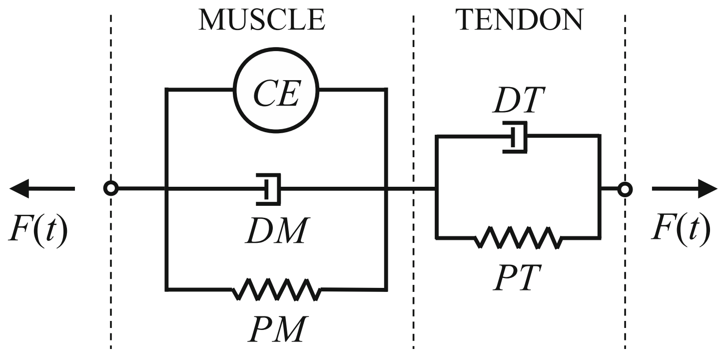
Scamnum: treatment of vertebral fractures and dislocations

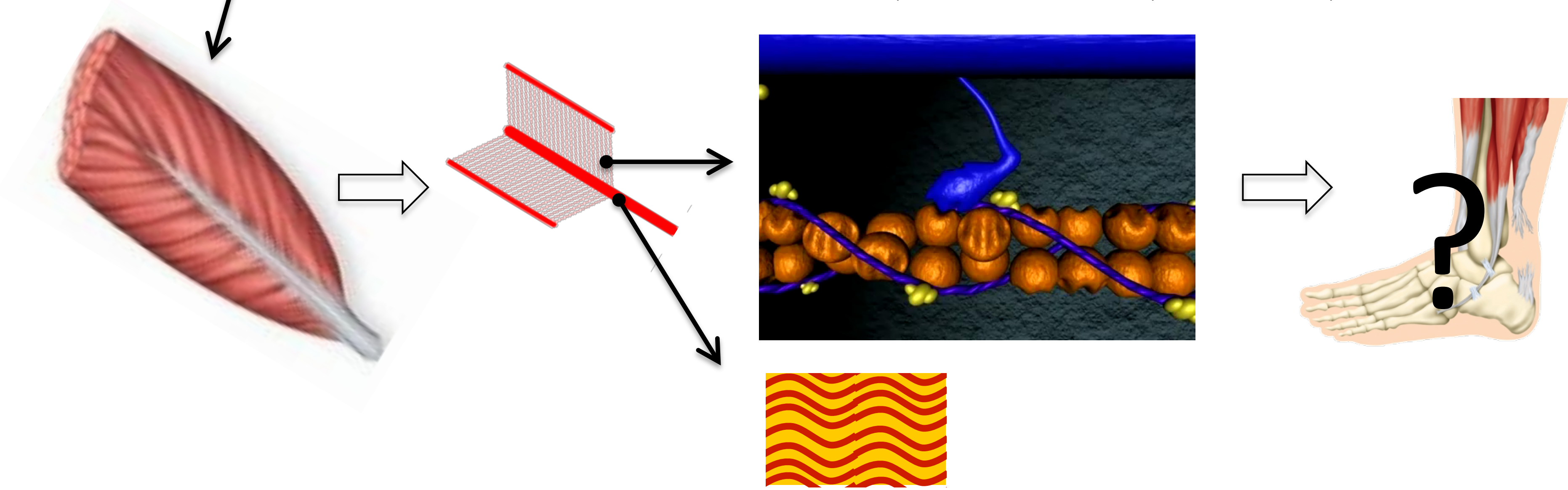
Biomechanics?

Models to predict the mechanics:

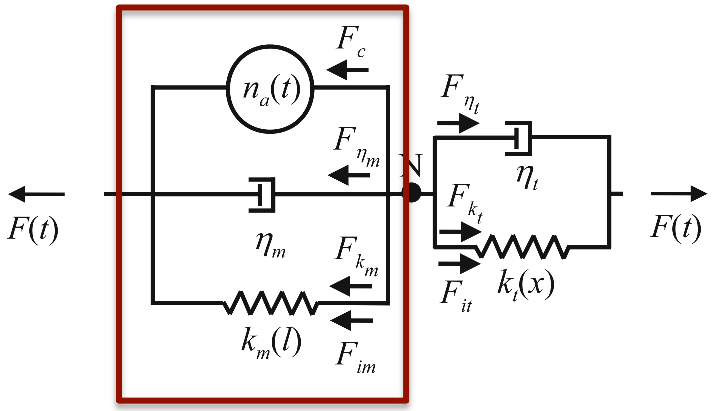
of biological structures

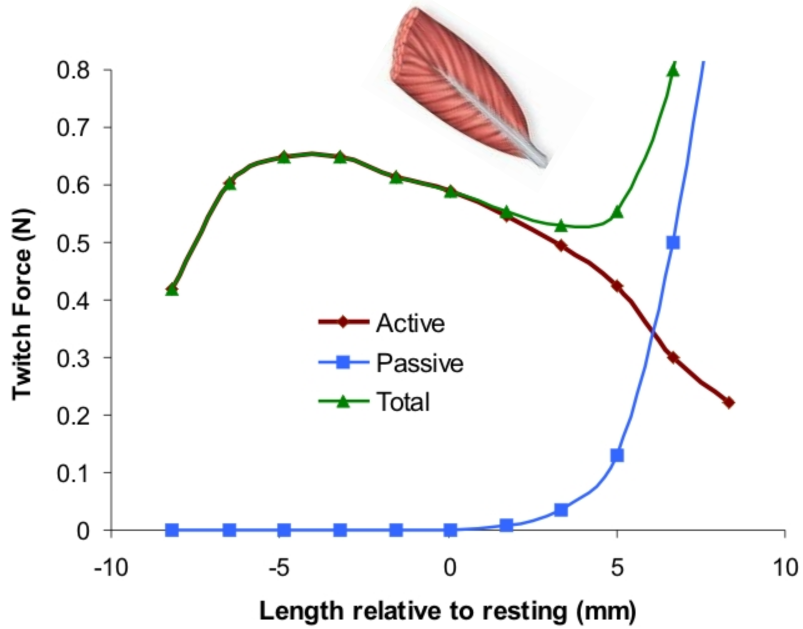
in biological structures





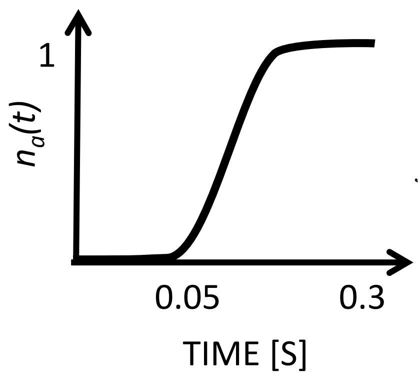
MUSCLE-TENDON UNIT





$$F_{k_m}(l) = k_m(l)(l - l_o) = \begin{cases} 0 & l < l_o \\ \frac{F_{\max}}{[\exp(C_{pe})-1]}\left[\exp\left(\frac{C_{pe}}{C_{pm}}\frac{l-l_o}{l_o}\right) - 1\right] & l \geq l_o \end{cases}$$

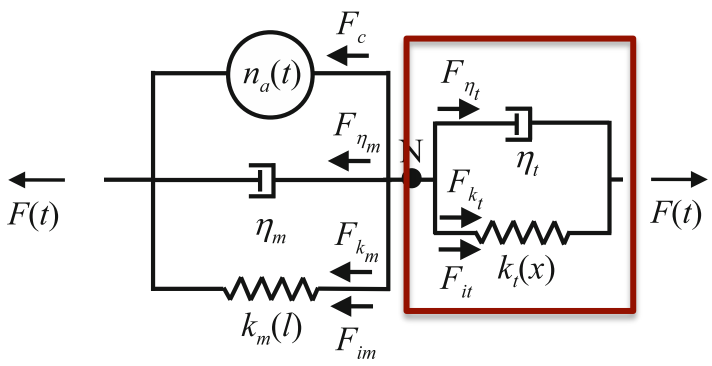
$$F_c(t, l, v) = F_{\max} \cdot n_a(t) \cdot f_\ell(l)$$

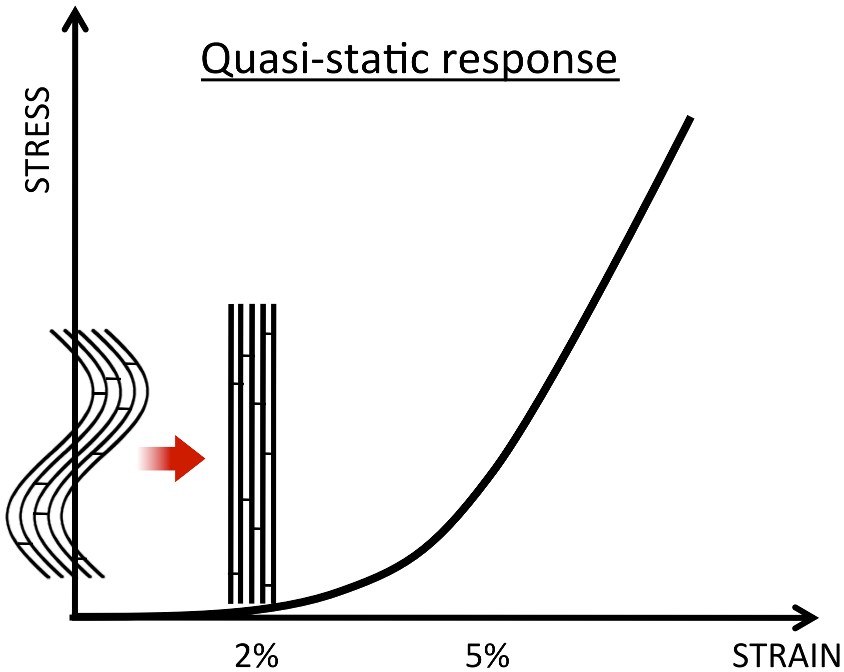


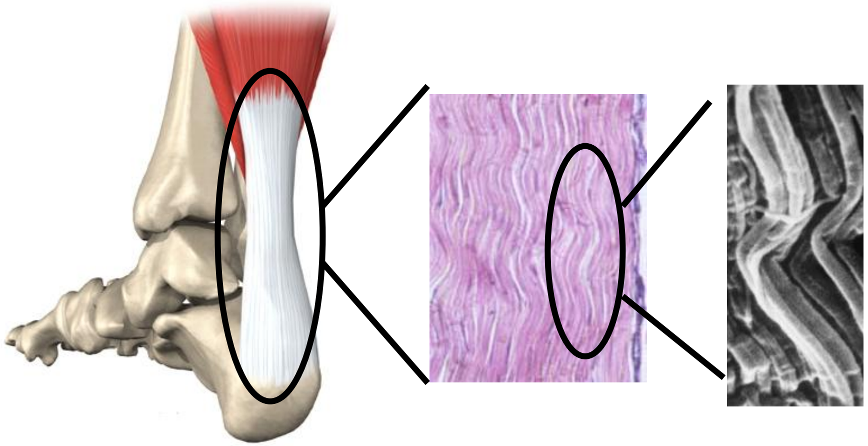
$$f_\ell(l) = \exp\left[-\left(\frac{l - l_{opt}}{l_{opt} C_{sh}}\right)^2\right]$$

Wittek A, Kajzer J, Haug E (2000) Hill-type muscle model for analysis of mechanical effect of muscle tension on the human body response in a car collision using an explicit finite element code. *Jpn Soc Mech Eng Int J Ser A 43:8–18*

MUSCLE-TENDON UNIT

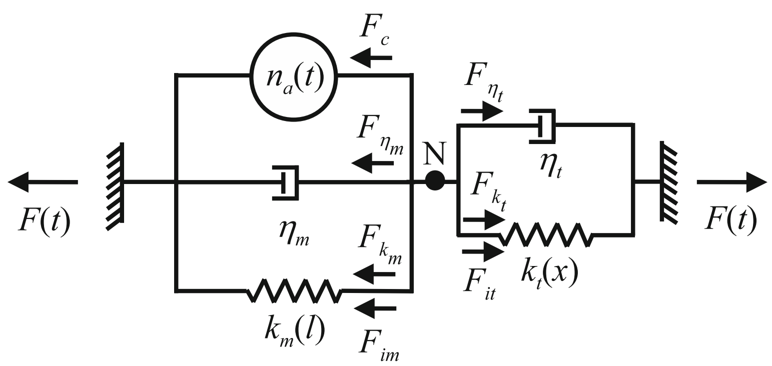




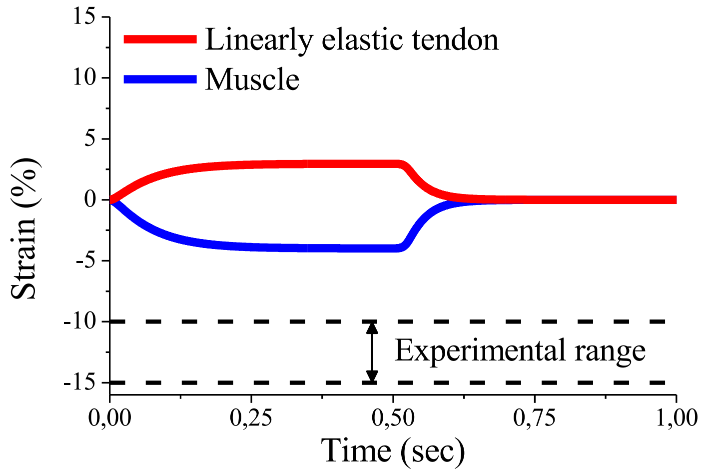


MUSCLE-TENDON UNIT

Is muscle mechanics affected by tendinous non-linearities?



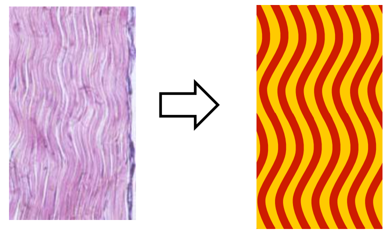
F. Maceri, **M. Marino**, **G. Vairo** (2012) An Insight on Multiscale Tendon Modelling in Muscle-Tendon Integrated Behaviour, *Biom Model Mechanobiol 11*



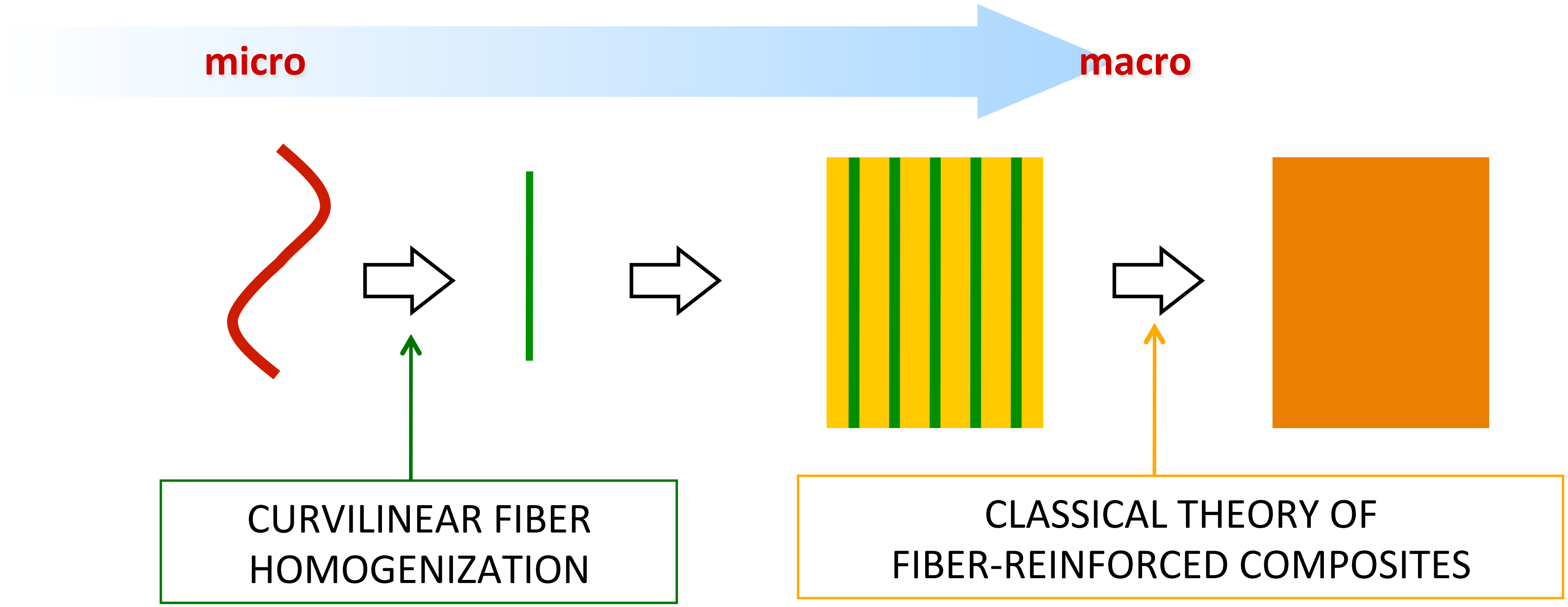
Muscular compliance not reproduced

Muscular force is clearly altered

Tissue: *Model:*



Double homogenization step



WHY MULTISCALE?

STRUCTURE → MECHANICS

The need of a constitutive relationship at the **MACROSCALE:**

The mechanical performance of locomotor system highly depend on tendinous mechanics

BUT

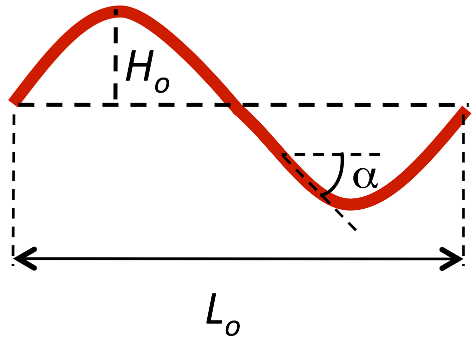
CAUSE AT THE MICROSCALE ⇨ **MACROSCOPIC EFFECT**

Alteration of fiber crimp (e.g., scars)

Alteration of volumetric fraction (e.g., Ehlers-Danlos syndrome)

⇨ Stiffening/laxity and higher rupture risks

MICRO MECHANICS



$f(x)=H_o\sin(2\pi x/L_o)$

- Beam theories

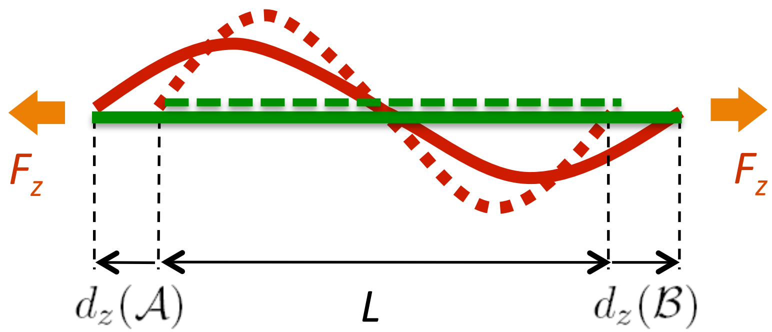
Frish-Fay, Flexible Bars, Butterworths 1962.

- Asymptotic expansion homogenization methods

M. Potier-Ferry, L. Said, "Geometrical homogenization of a corrugated beam", *Comptes Rendus de l'Académie des Sciences* 314, 1992.

- Energetic approach

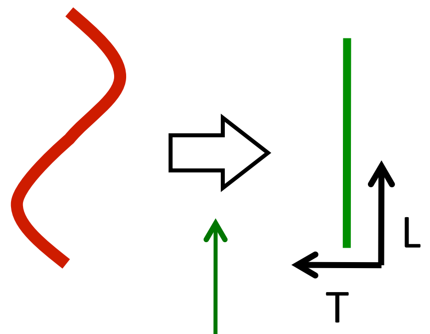
M. Marino, G. Vairo, "Equivalent Stiffness and Compliance of Curvilinear Elastic Fibers", In: *Mechanics, Models and Methods in Civil Engineering* 61, 2012.



$$\varepsilon_F = \frac{d_z(\mathcal{B}) - d_z(\mathcal{A})}{L} \qquad F_z = (EA)_{eq}\,\varepsilon_F$$

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

MICRO MECHANICS



CURVILINEAR FIBER HOMOGENIZATION

$$E_{eq}(\varepsilon_F) = E_\ell I_F \langle \cos\alpha \rangle \left[I_F \langle \cos^2\alpha \rangle + A_F \langle f(x,\varepsilon_F)^2 \rangle \right]^{-1}$$

Linearly elastic isotropic matrix

E_M, ν_M

Transversely isotropic fiber:

$$E_{F,\,L}(\varepsilon_F) = E_{eq}(\varepsilon_F), \qquad E_{F,\,T} = E_M,$$
$$\nu_{F,\,LT} = \nu_{F,\,TT} = \nu_M, \qquad G_{F,\,LT} = E_M/[2(1+\nu_M)],$$

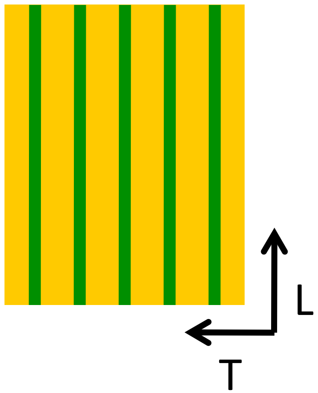
Collagen volume fraction: V_f

Mixture rule

$$E_L(\varepsilon_F) = V_f E_{F,\,L}(\varepsilon_F) + (1-V_f)E_M, \qquad E_T = \frac{E_{F,\,T}E_M}{E_{F,\,T}(1-V_f)+E_M V_f},$$
$$G_{LT} = \left(\frac{V_f}{G_{F,\,LT}} + \frac{1-V_f}{G_M} \right)^{-1}, \qquad G_{TT} = \left(\frac{V_f}{G_{F,\,TT}} + \frac{1-V_f}{G_M} \right)^{-1},$$
$$\nu_{LT} = V_f \nu_{F,\,LT} + V_m \nu_M, \qquad \nu_{TT} = \frac{E_T}{2G_{TT}} - 1,$$

MACRO MECHANICS

- TRANSVERSELY ISOTROPIC MATERIAL IN LOCAL FRAME



$$[\mathbb{L}] = \frac{1}{D}\begin{bmatrix} E_L(1-\nu_{TT}^2) & E_T\nu_{LT}(1+\nu_{TT}) & E_T\nu_{LT}(1+\nu_{TT}) \\ E_T\nu_{LT}(1+\nu_{TT}) & E_T(1-\frac{E_T}{E_L}\nu_{LT}^2) & E_T(\nu_{TT}+\frac{E_T}{E_L}\nu_{LT}^2) \\ E_T\nu_{LT}(1+\nu_{TT}) & E_T(\nu_{TT}+\frac{E_T}{E_L}\nu_{LT}^2) & E_T(1-\frac{E_T}{E_L}\nu_{LT}^2) \end{bmatrix}$$

$$[\mathbb{M}] = \begin{bmatrix} \frac{E_T}{2(1+\nu_{TT})} & 0 & 0 \\ 0 & G_{LT} & 0 \\ 0 & 0 & G_{LT} \end{bmatrix} \qquad D = 1-\nu_{TT}^2-2(1+\nu_{TT})\frac{E_T}{E_L}\nu_{LT}^2$$

$$[\mathbb{C}^L] = \begin{bmatrix} [\mathbb{L}] & [0] \\ [0] & [\mathbb{M}] \end{bmatrix}$$

In the global coordinate system: $[\mathbb{C}] = \left[\hat{\mathbb{T}}_\sigma\right]\left[\mathbb{C}^L\right]\left[\hat{\mathbb{T}}_\varepsilon\right]^{-1}$

Stress and strain transformation matrices

MICRO-MACRO MODEL

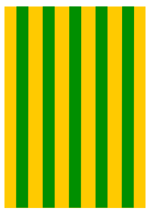
Few parameters, experimentally measurable

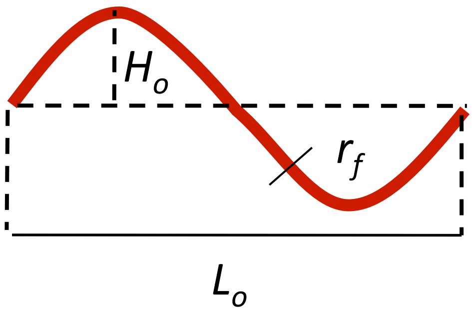
MECHANICAL PARAMETERS: E_M - E_c

GEOMETRIC PARAMETERS:

V_f → <u>MACRO</u>

r_f, L_o, H_o → <u>MICRO</u>



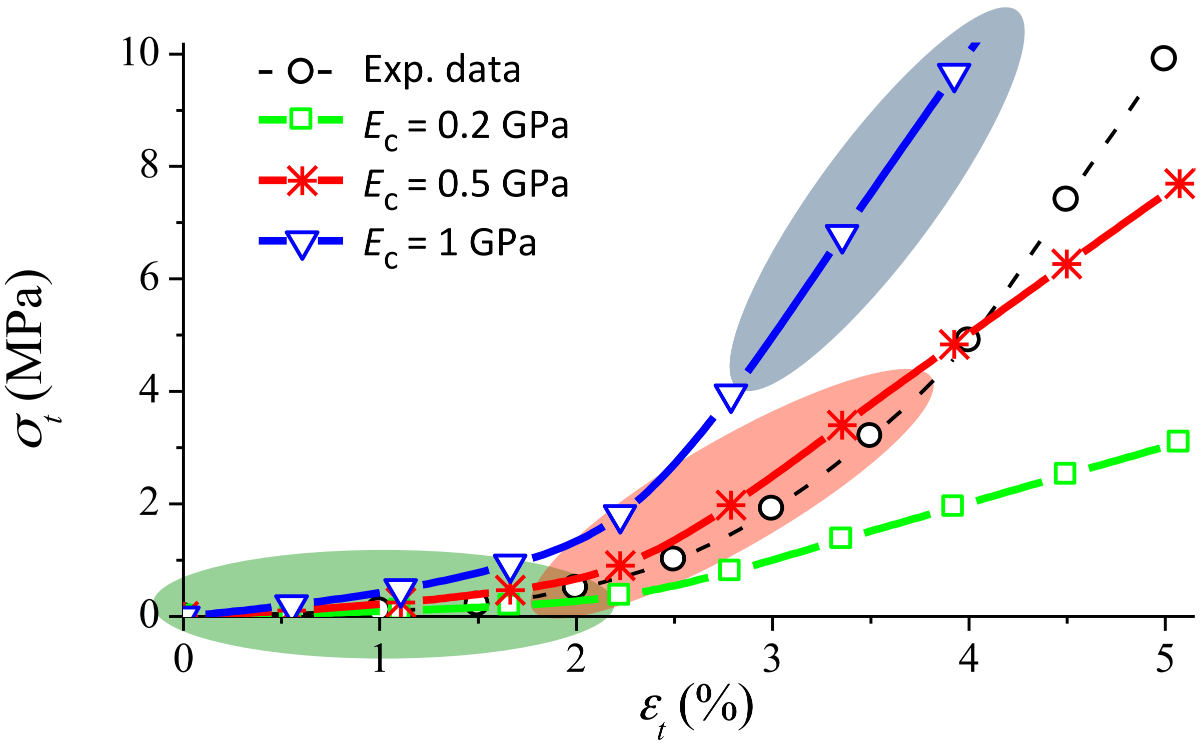


	Tendon	**Ref.**
L_o	240 μm	Hansen et al., 2002
H_o	10.8 μm	Maceri et al., 2009
r_f	4.0 μm	Kannus,2000
V_f	50%	Silver et al., 2001
ν_m	0.49	Lavagnino et al., 2008
E_M	1 MPa	Lavagnino et al., 2008

$\boxed{E_c : 0.1\text{-}40 \text{ GPa (Fratzl, 2008)}}$

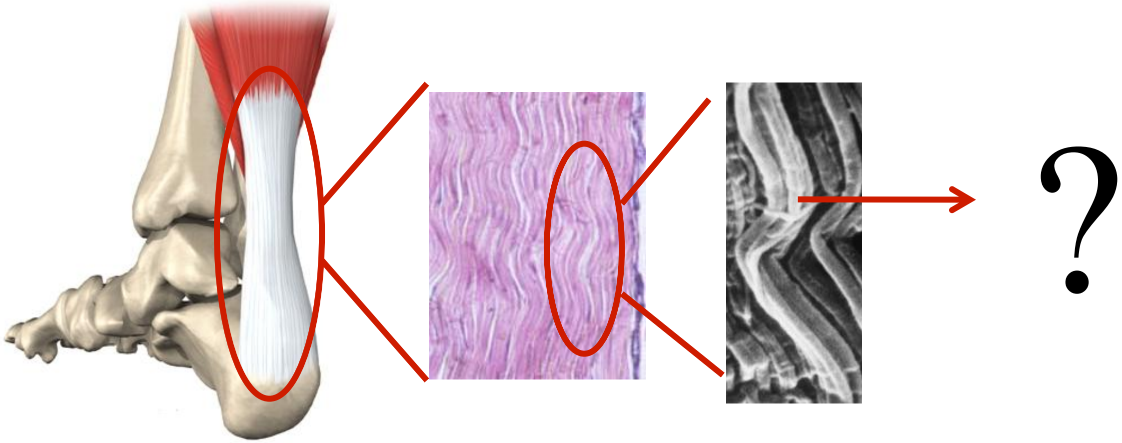
MICRO-MACRO MODEL: RESULTS

Non-constant collagen elastic modulus?

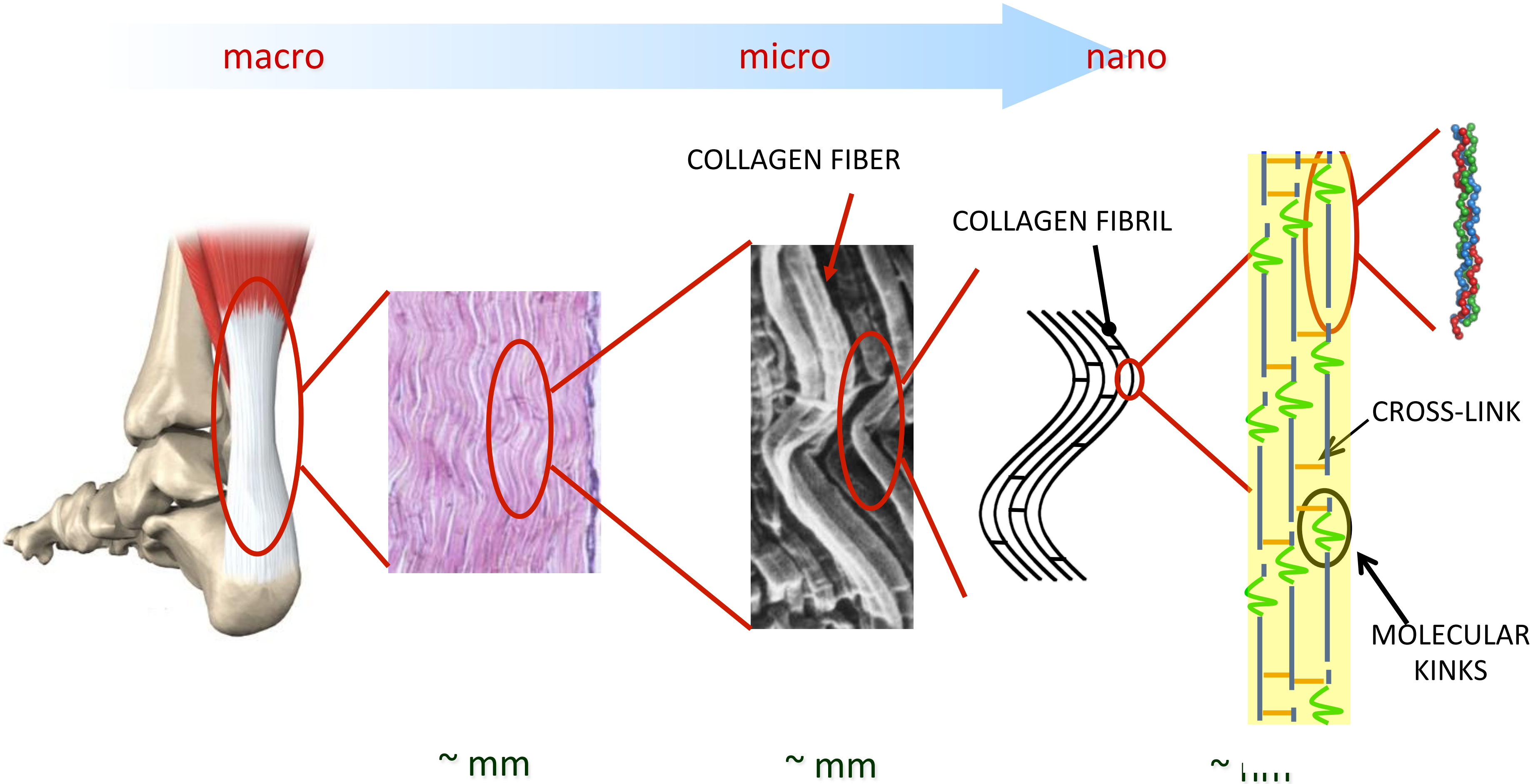



CHANCE

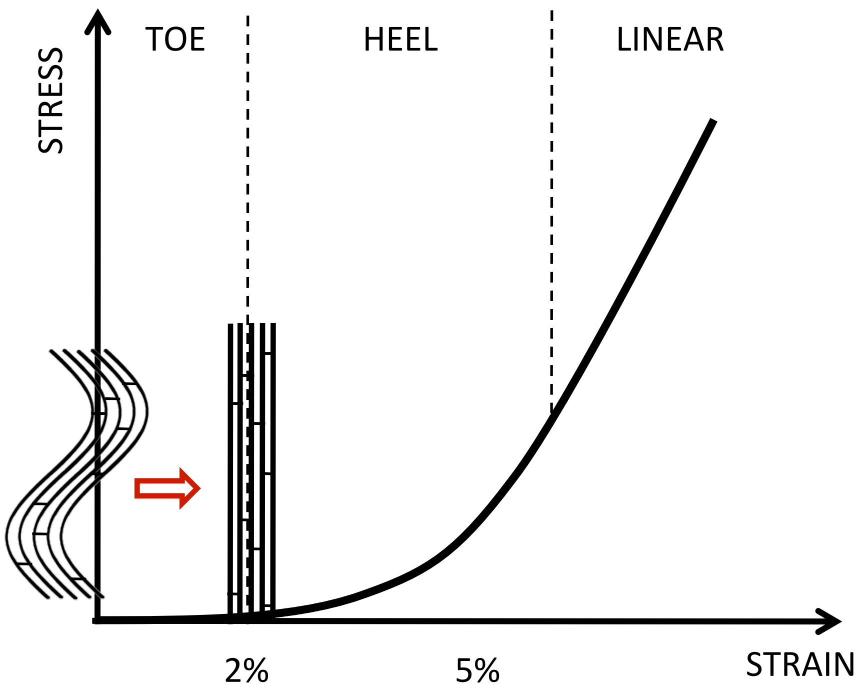

GO


?

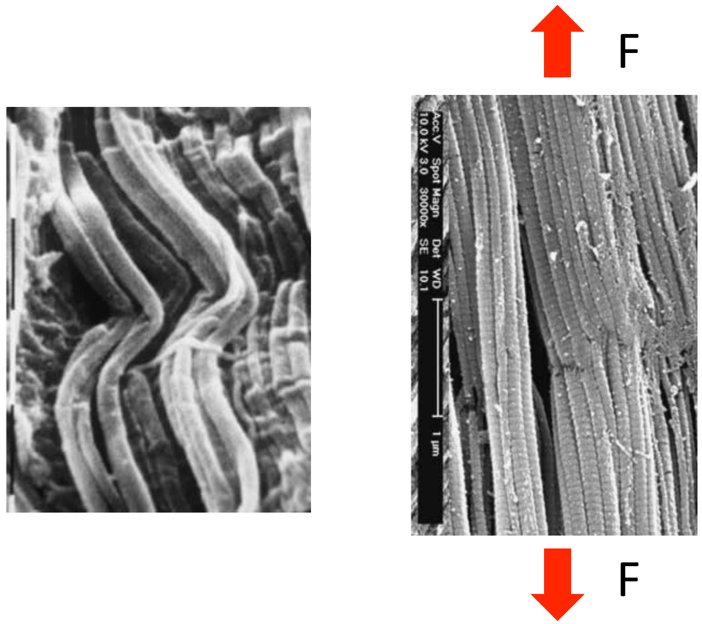
FROM MACRO TO NANO STRUCTURE



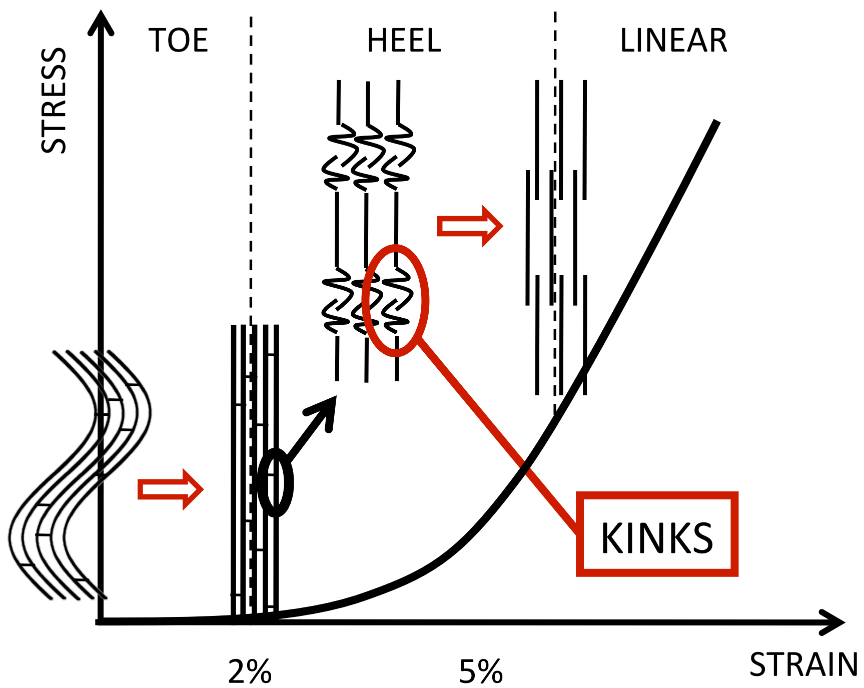
FROM MACRO TO NANO MECHANICS



"TOE REGION": microscopic crimp removal



FROM MACRO TO NANO MECHANICS

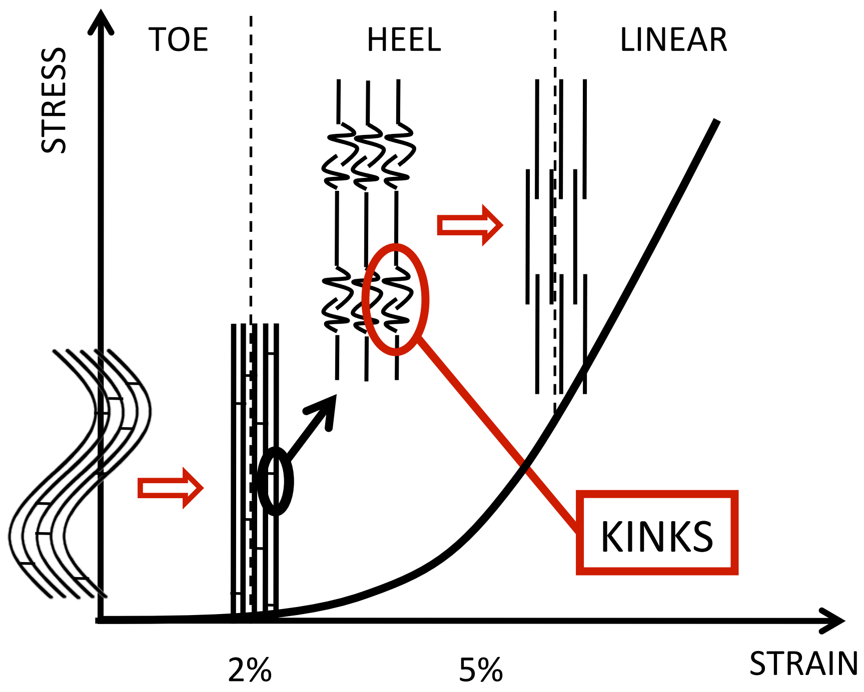


"TOE REGION": microscopic crimp removal

↓

"HEEL REGION": molecular kinks straightening (entropic mechanisms)

FROM MACRO TO NANO MECHANICS



"TOE REGION": microscopic crimp removal

↓

"HEEL REGION": molecular kinks straightening (entropic mechanisms)

↓

"LINEAR REGION": molecular and cross-links straightening

WHY MULTISCALE?

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The mechanical performance of locomotor system highly depend on tendinous mechanics

BUT

NON MACRO CAUSE ⇨ **MACROSCOPIC EFFECT**

MICROSCALE:

Histological alteration ⇨ Altered mechanical response

NANOSCALE:

Genetic defects ⇨ Laxity (articular hyper-extensibility)

Decrease of cross-links ⇨ Higher rupture risks

Analysis and modeling of tissue mechanics at different length scales allow to understand a number of physio-pathological processes

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The mechanical performa ... mechanics

NON MACRO CA ... T

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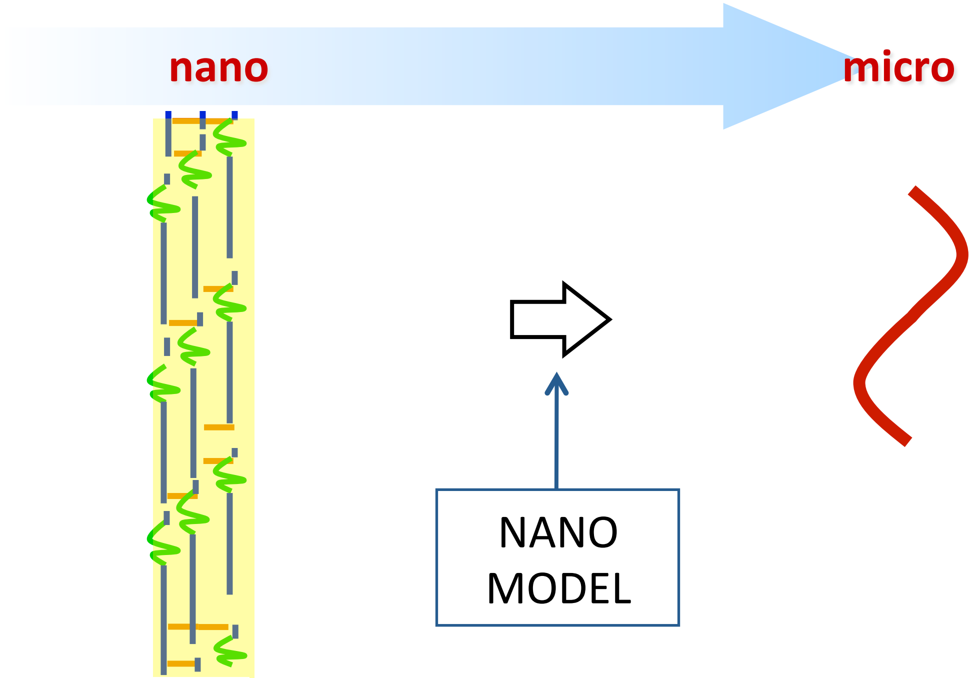
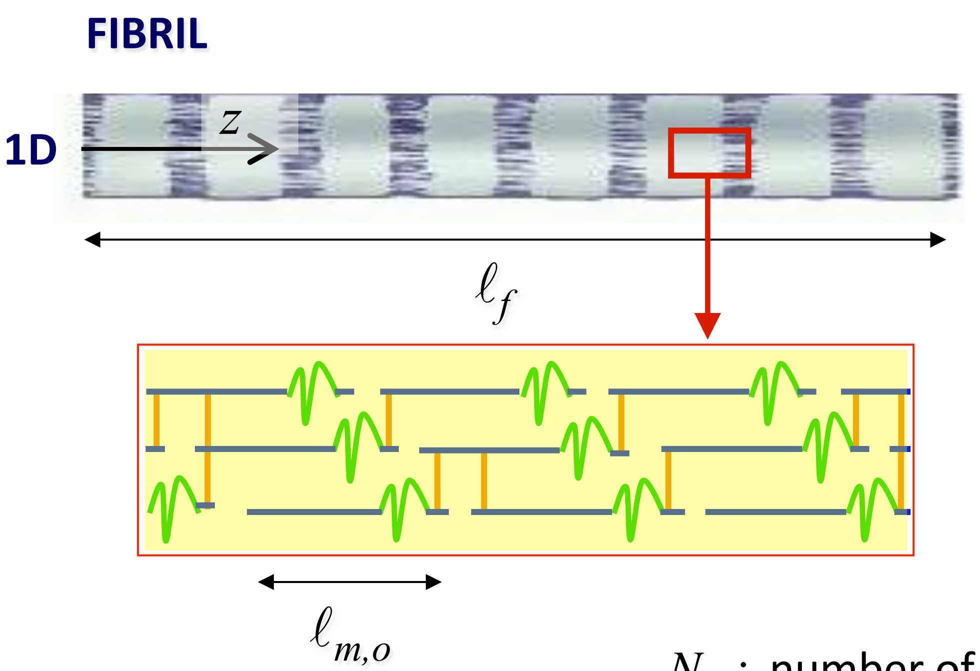
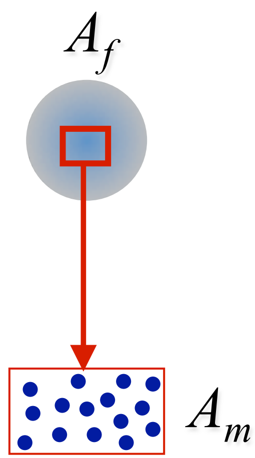
> *Analysis and modeling of tissue mechanics at different length scales allow to understand a number of physio-pathological processes*

NANO-MICRO HOMOGENIZATION



NANO STRUCTURE





$$N_a = A_c / A_m$$
$$A_c \approx 0.7 A_f$$

z : material symmetry axis for fibril

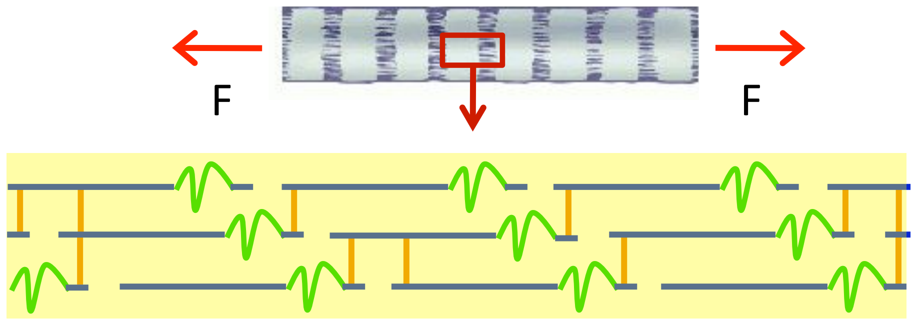
N_m : number of molecules

n_i^c : number of cross-links acting upon the ith molecule

$\lambda = \sum_{i=1}^{N_m} n_i^c / (2N_m)$: average covalent-bonds occurrence

$N_c = \lambda N_m$: total number of covalent bonds

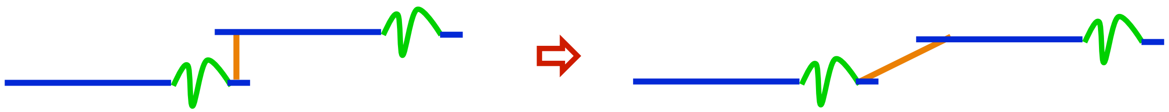
NANO MECHANICS



KINEMATICS: Two deformation mechanisms

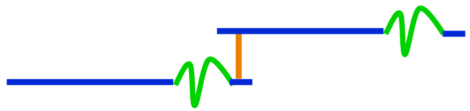
- Molecular straightening:

- Cross-links straightening:



CONSTITUTIVE RESPONSE

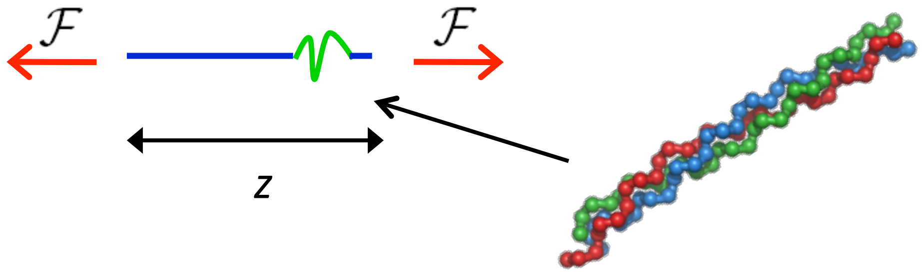
Non-linearly elastic (E_m)

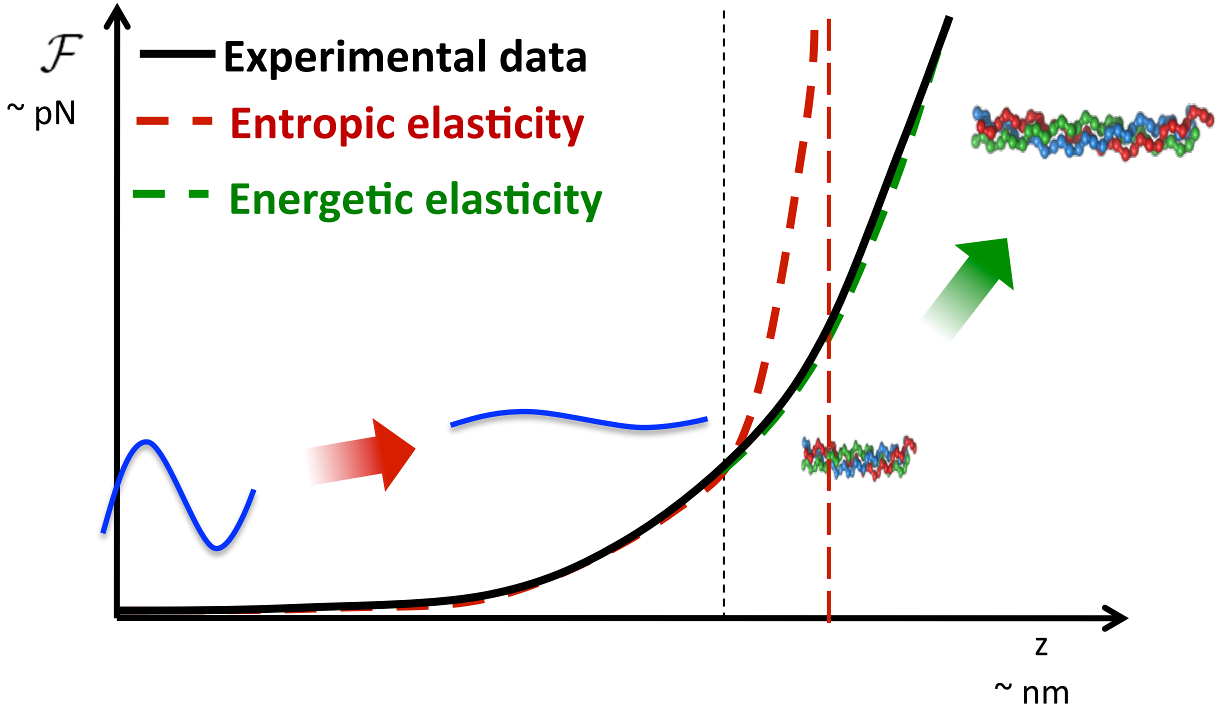


Linearly elastic (k_{cl})

NANO MECHANICS: COLLAGEN

Atomic Force Microscopy:





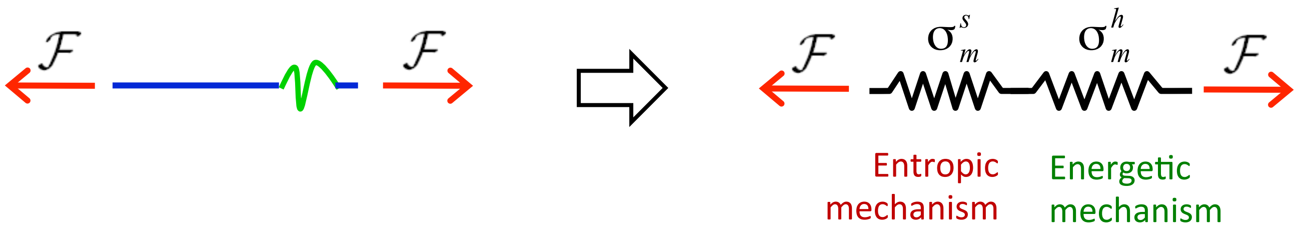
Unrolling of triple helices and covalent bonds stretching

Bozec (2005)

Bozec (2005)

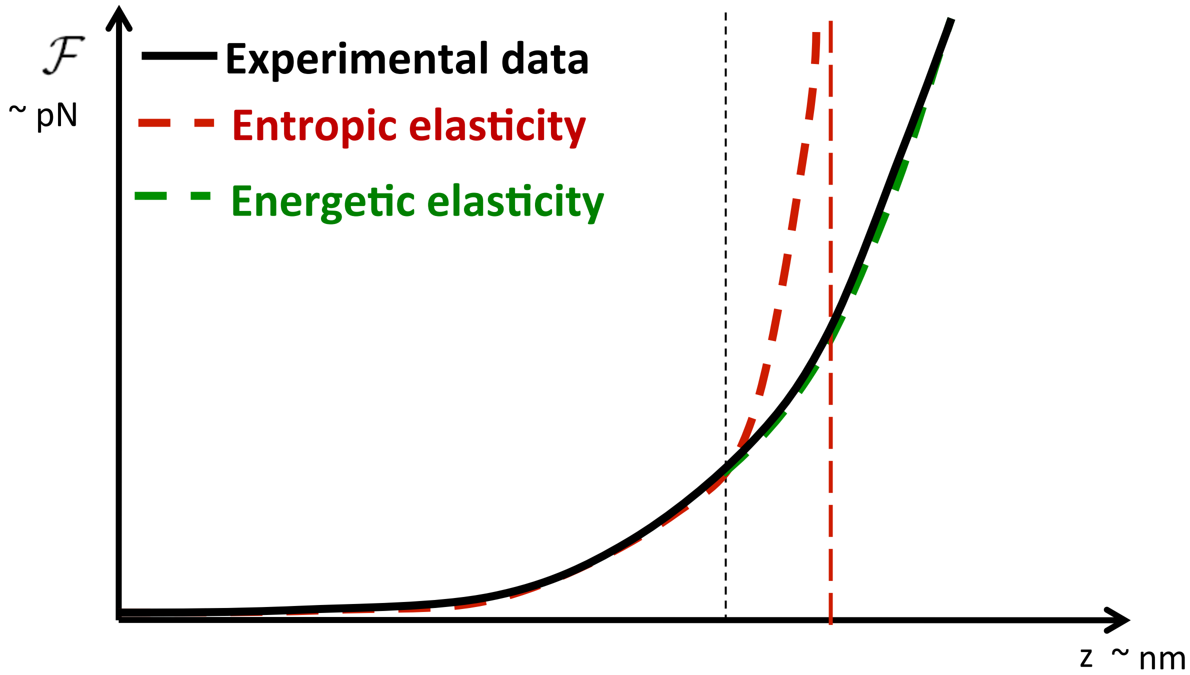
Maceri, Marino, Vairo (2012)

NANO MECHANICS: COLLAGEN

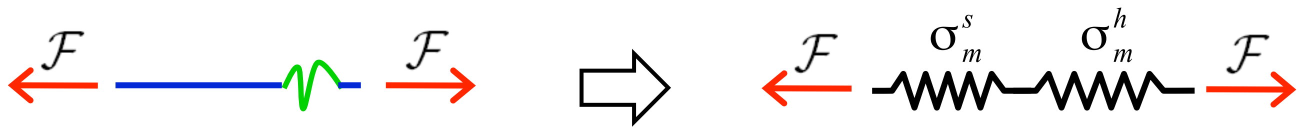


$$\sigma_m(\varepsilon_m) = \frac{\mathcal{F}}{A_m}$$

$$\varepsilon_m = \varepsilon_m^s + \varepsilon_m^h$$



NANO MECHANICS: COLLAGEN



Entropic mechanism

Energetic mechanism

$$\sigma_m(\varepsilon_m) = \frac{\mathcal{F}}{A_m}$$

$$\varepsilon_m = \varepsilon^s_m + \varepsilon^h_m$$

Tangent elastic modulus in entropic elasticty:

$$E^s_m = \frac{\varrho}{A_m}\left\{\frac{r_\ell}{2[1-r_\ell(1+\varepsilon^s_m)]^3} + r_\ell\right\}$$

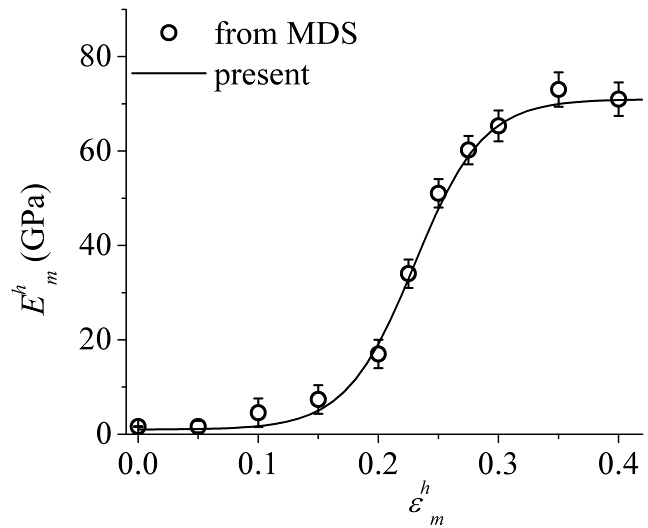
Recovery of the classical Worm-like chain formulation (Marko and Siggia, 1995)

$$r_\ell = \frac{\ell_m}{\ell_c}$$

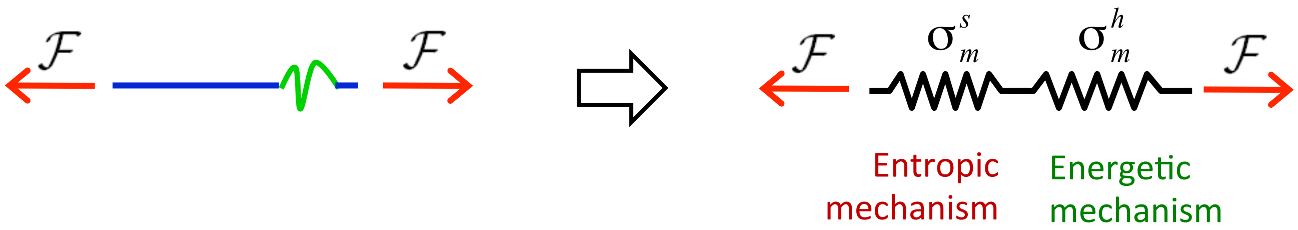
Tangent elastic modulus in energetic elasticity

$$E^h_m(\varepsilon^h_m) = \frac{\hat{E} r_\ell}{1+e^{-k(r_\ell\varepsilon^h_m - \varepsilon^h_o)}} + \hat{E}_o r_\ell$$

No … helices … 012)



NANO MECHANICS: COLLAGEN



$$\sigma_m(\varepsilon_m) = \frac{\mathcal{F}}{A_m}$$

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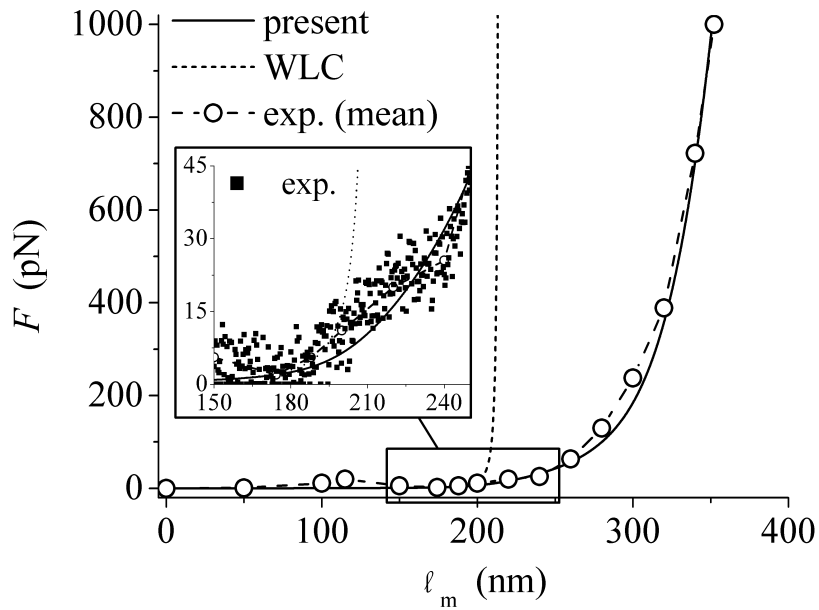
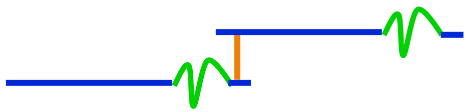


$$E_m(\varepsilon_m) = \frac{E_m^s(\varepsilon_m^s)E_m^h(\varepsilon_m^h)}{E_m^s(\varepsilon_m^s) + E_m^h(\varepsilon_m^h)}$$

F. Maceri, M. Marino, G. Vairo "Elasto-damage modeling of biopolymer molecules response", *Computer Modeling in Engineering and Sciences* 87, 2012

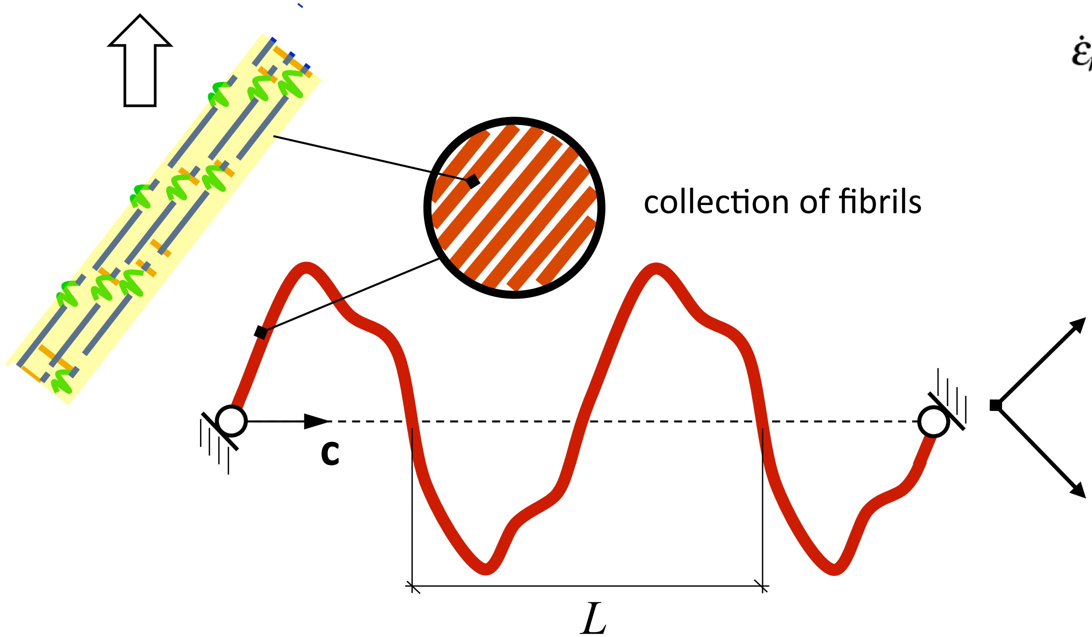
MULTISCALE APPROACH

$$E_f(\varepsilon_f) = \mu \left[\frac{1}{E_m(\varepsilon_m)} + \frac{A_m}{\lambda k_{cl} \ell_{m,o}} \right]^{-1}$$



Compatibility solved by the differential problem

$$\dot{\varepsilon}_m = \frac{E_f(\varepsilon_f)}{\mu E_m(\varepsilon_m)} \dot{\varepsilon}_f$$



MATERIAL NON-LINEARITIES

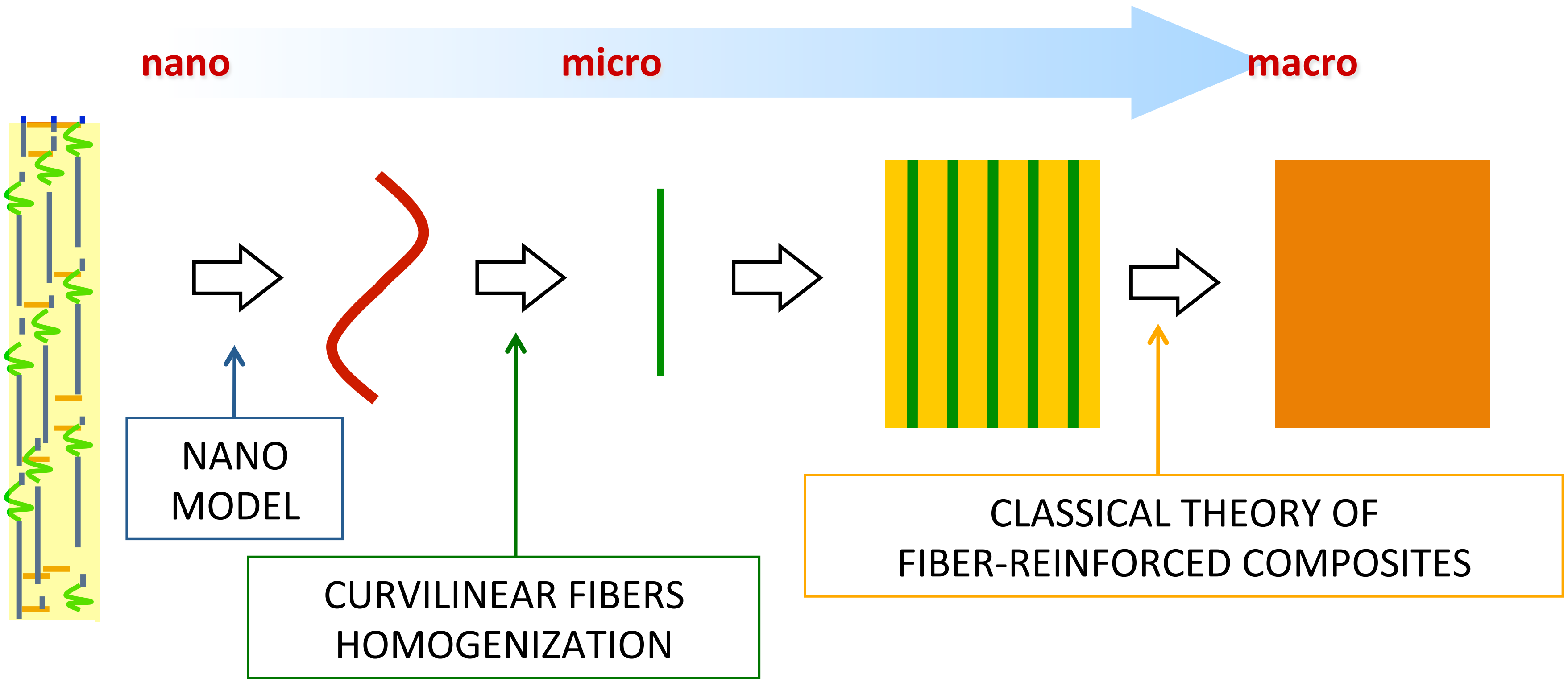
GEOMETRIC NON-LINEARITIES

$$E_{eq}(\varepsilon_F) = E_\ell I_F \langle \cos\alpha \rangle \left[I_F \langle \cos^2\alpha \rangle + A_F \langle f(x,\varepsilon_F)^2 \rangle \right]^{-1}$$

with $E_\ell = E_f(\varepsilon_f)$

M. Marino, G. Vairo, "Multiscale Elastic Models of Collagen Bio-structures: From Cross-Linked Molecules to Soft Tissues", In: *Multiscale Computer Modeling in Biomechanics and Biomedical Engineering*, Springer 2013.

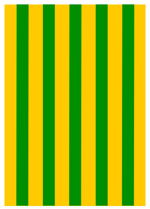
TENDON MODEL



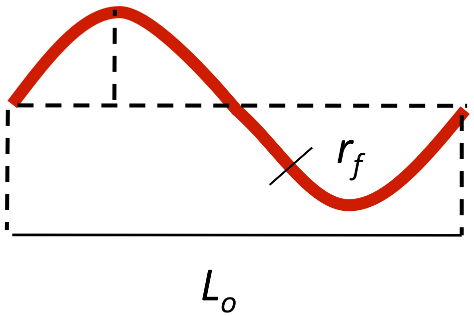
TENDON MODEL

Few parameters, experimentally measurable

V_f
E_M
MACRO

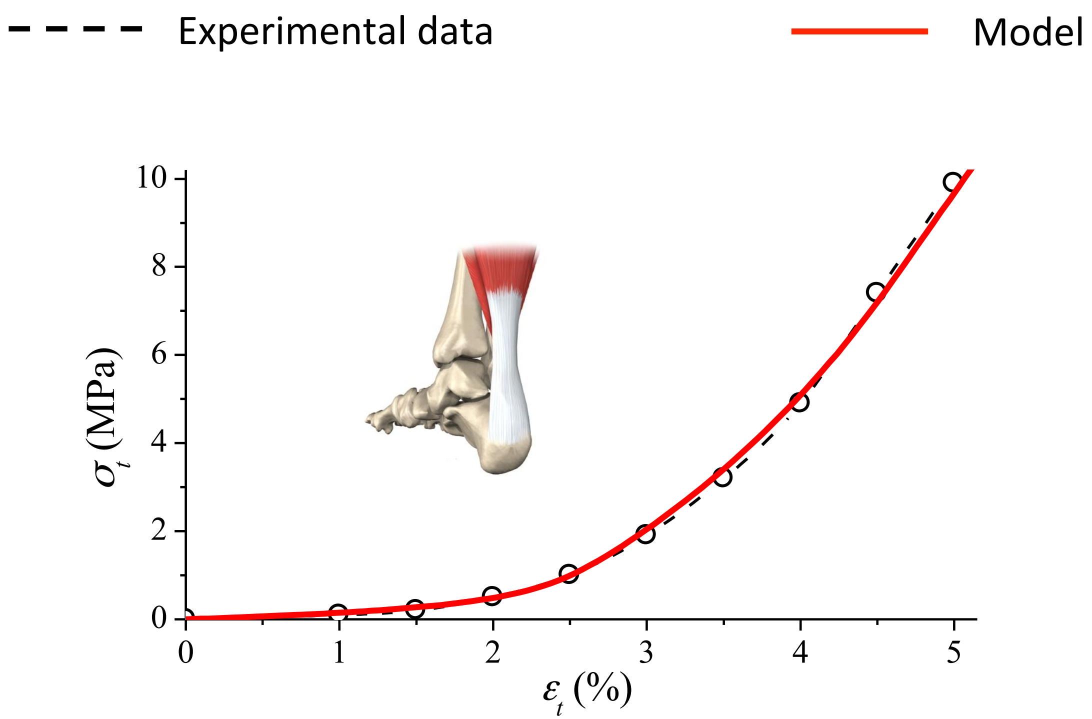


r_f
L_o
H_o
MICRO



λk_{cl}
Molecular parameters
NANO

TENDON MODEL: VALIDATION



F. Maceri, M. Marino, G. Vairo, "A unified multiscale mechanical model for soft collagenous tissues with regular fiber arrangement", *Journal of Biomechanics* 43, 2010.

TENDON MODEL: APPLICATION

Experimental data on 6 different subjects obtained by means of ultrasonic non-invasive techniques

P.M.H. Rack, D.R. Westbury, "Elastic properties of the cat soleus tendon and their functional importance", *J. Physiol 347, 1984.*

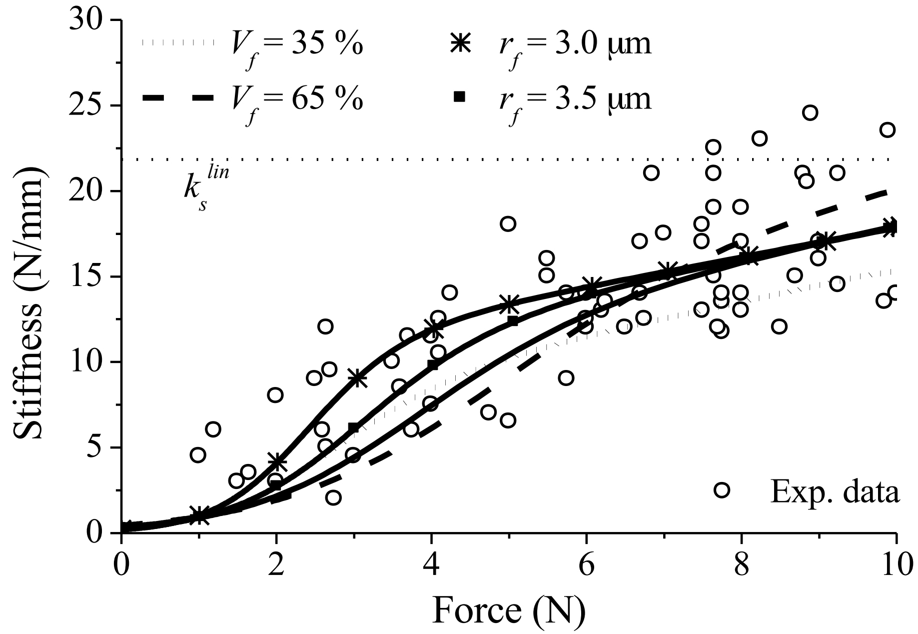
Non-invasive techniques

Predictive model

Inverse approach

DIAGNOSIS

TERAPEUTIC INDICATIONS



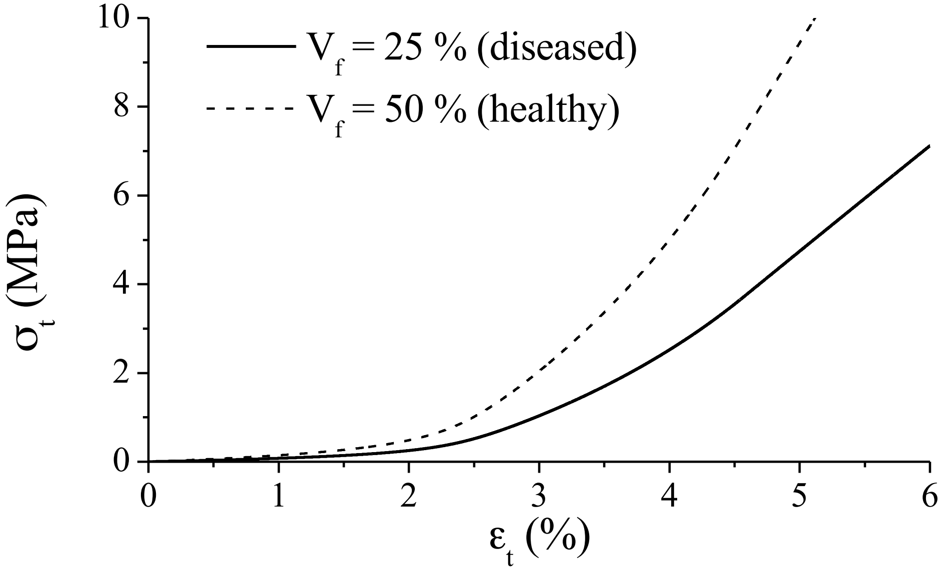
TENDON MODEL: APPLICATION

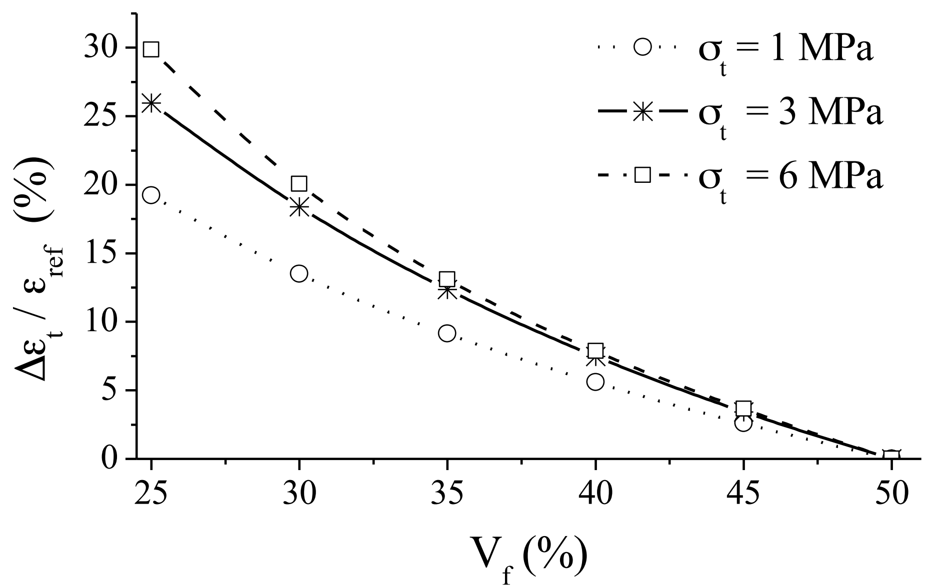
Disorder in collagen metabolism
(e.g., Ehlers-Danlos Syndrome)

Reduction of collagen content
(Mao et al., 2002)

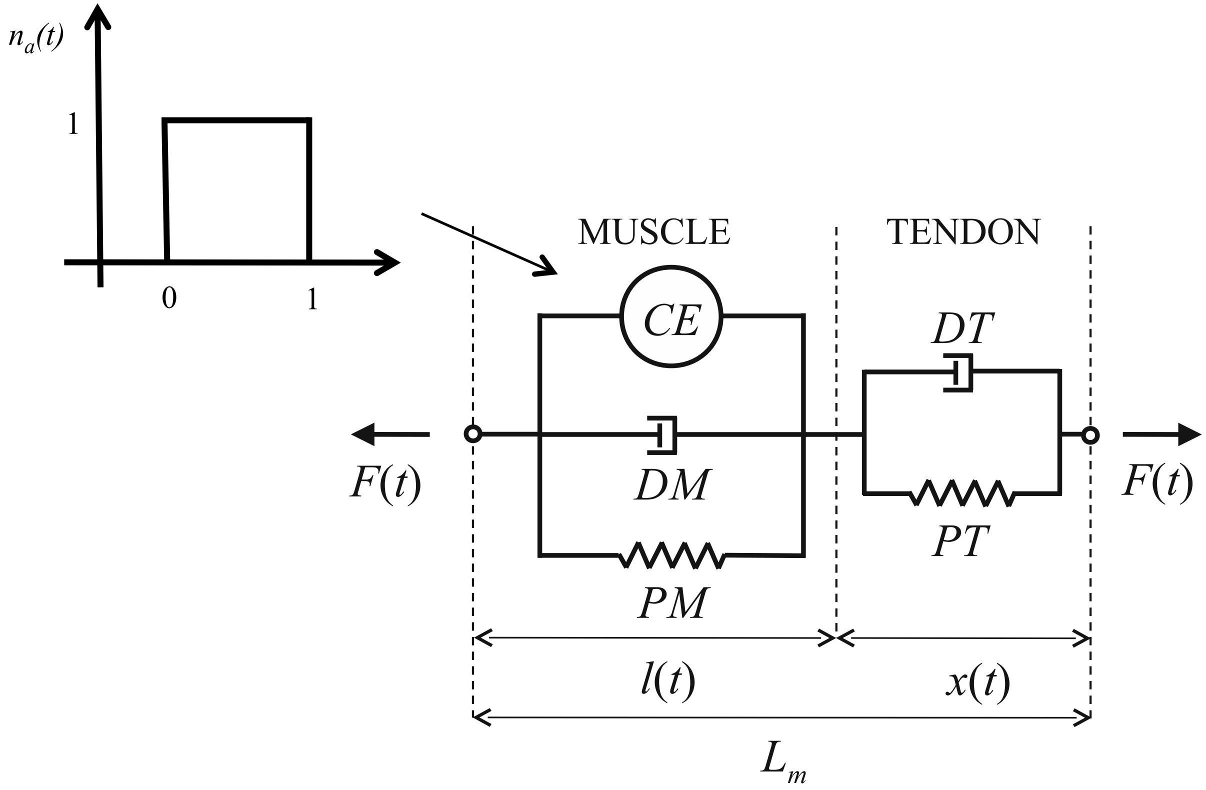
MODEL

Tissue hyper-extensibility
(Mao and Bristow, 2001)

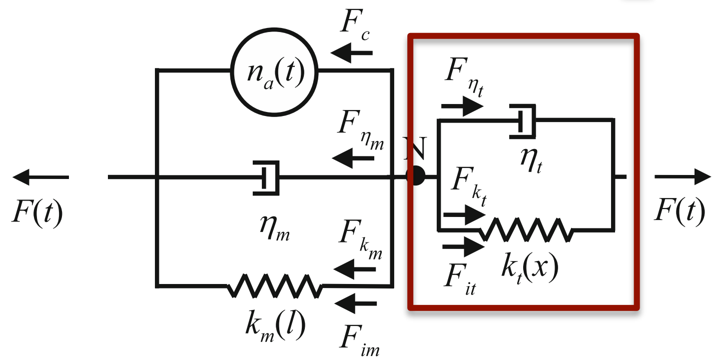




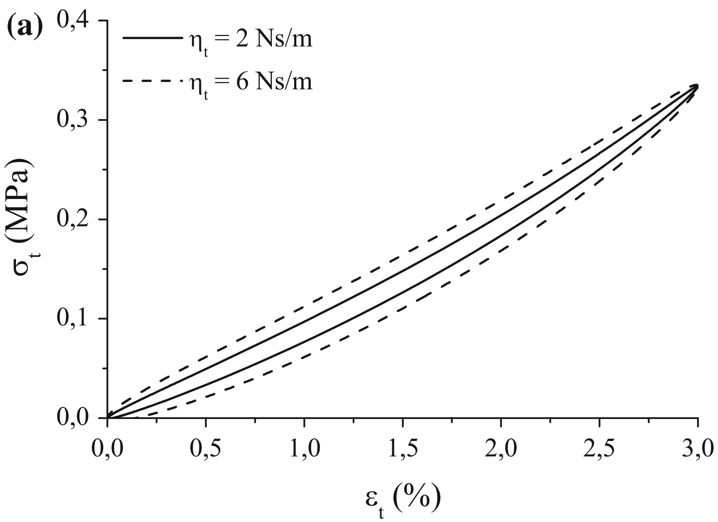
RESULTS

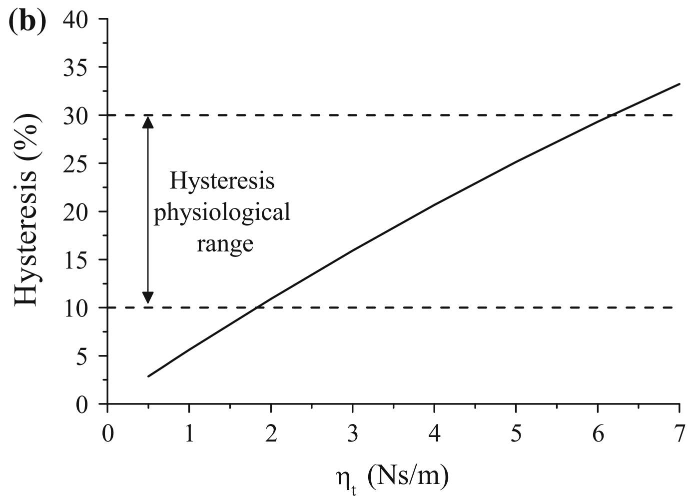


RESULTS

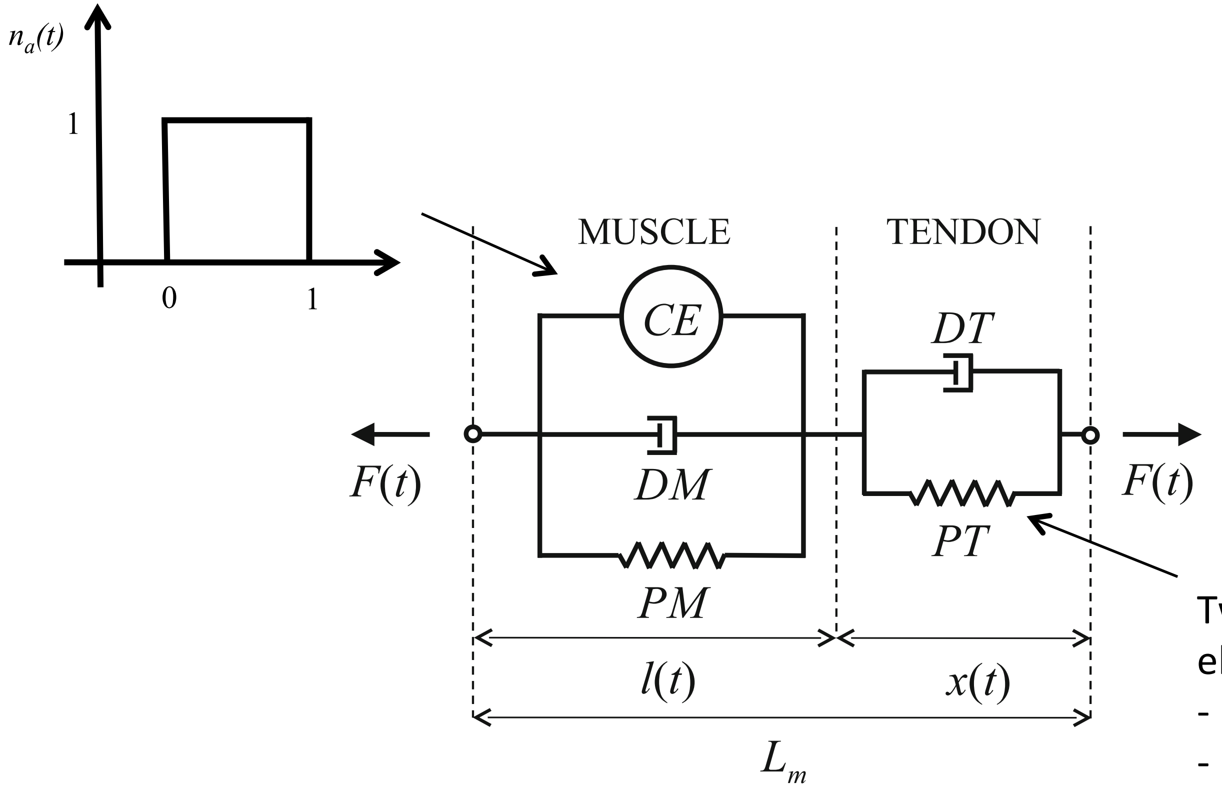


After the validation of the elastic behavior, viscous properties are defined by means of experimental results on the hysteresis cycle





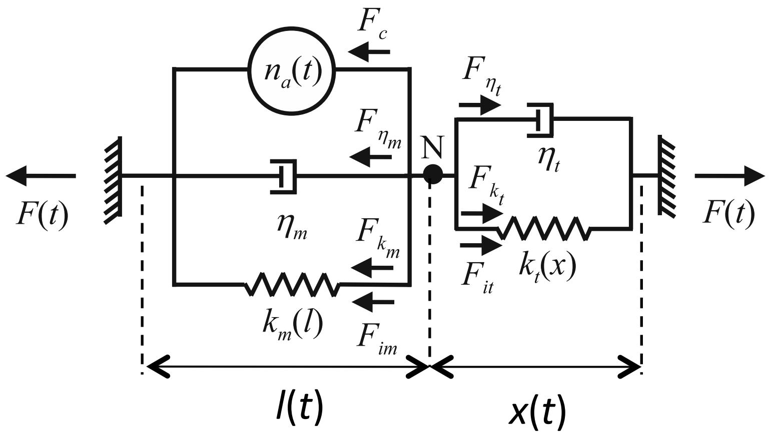
RESULTS

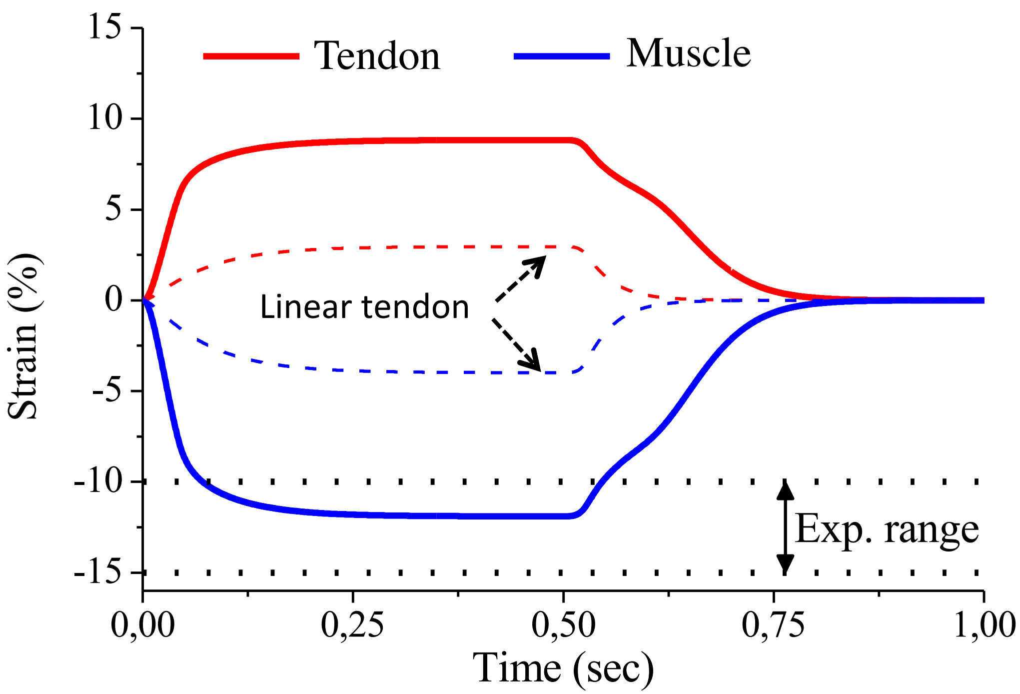


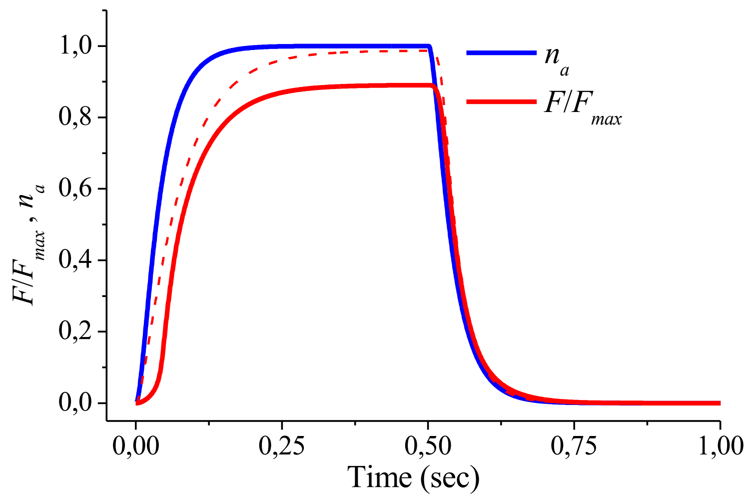
Two approaches for tendon elastic modeling:
- Linear approach
- Multiscale model
  (non-linear)

RESULTS

Muscular compliance is correctly reproduced only if coupled with a refined non-linear **tendon** modeling







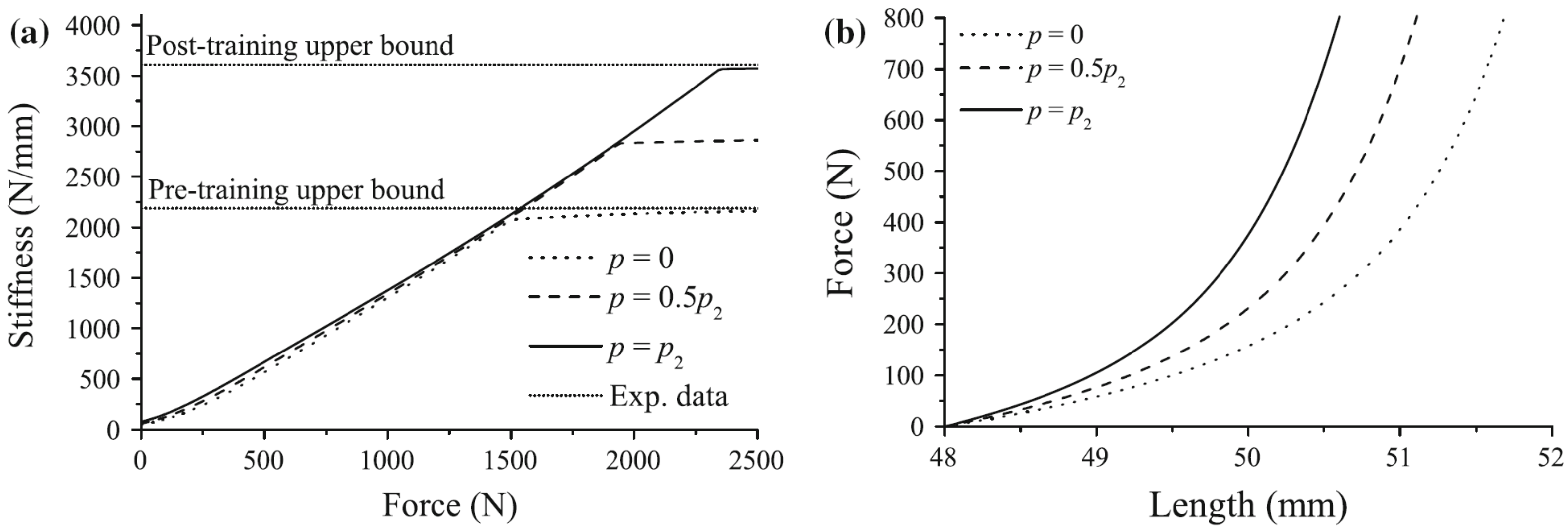
RESULTS

Training

Cross-link density alteration
Fiber crimp reduction
(Miles et al. 1992; Buchanan and Marsh 2002; Reeves et al. 2003a)

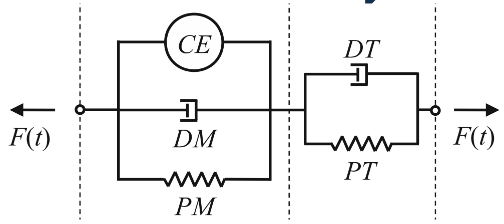
MODEL

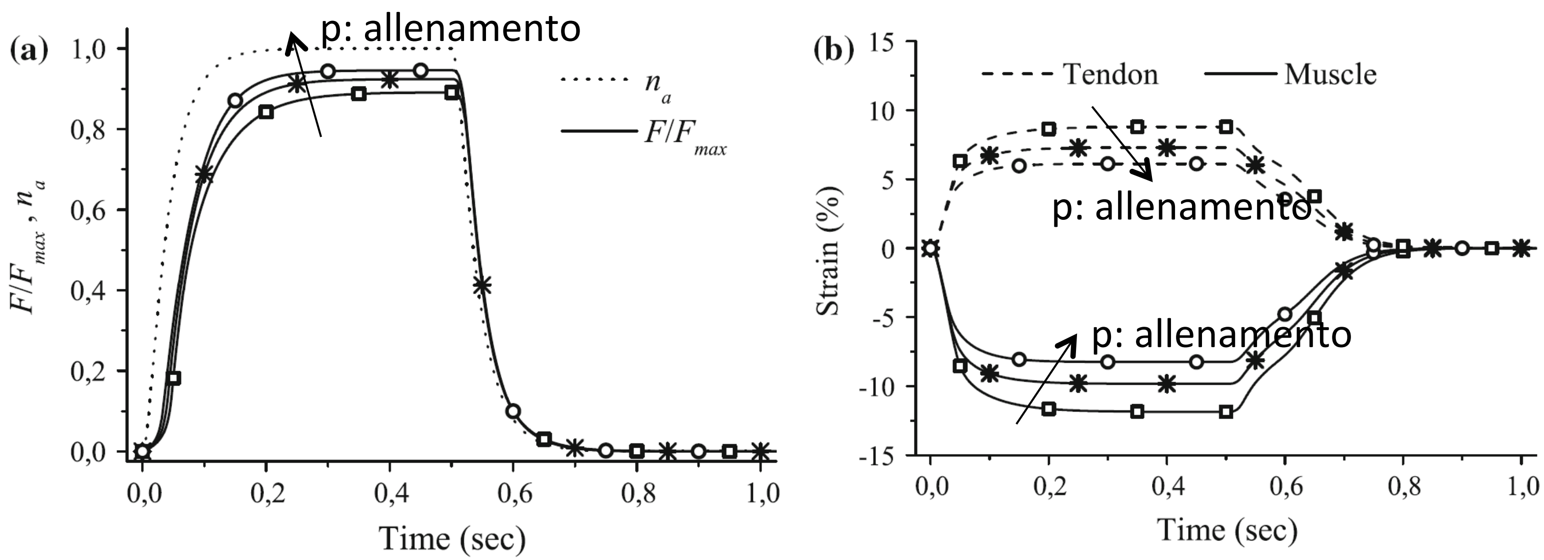
Tendon stiffening
(Maganaris et al., 2004)



RESULTS

Biological alterations → MODEL → Effects on tendon → MODEL → Effects on muscular functionality





MINI-COURSE

Mechanical modeling of soft biological tissues

Lesson 2 *Multiscale modeling of aorta mechanics and damage mechanisms*

… to be continued

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