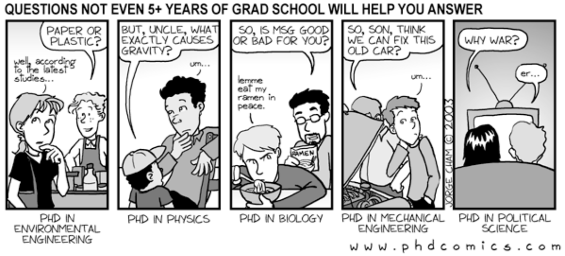
17 - examples - remodeling



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growth, remodeling and morphogenesis

growth [groʊθ] which is defined as added mass, can occur through cell division (hyperplasia), cell enlargement (hypertrophy), secretion of extracellular matrix, or accretion @ external or internal surfaces. negative growth (atrophy) can occur through cell death, cell shrinkage, or resorption. in most cases, hyperplasia and hypertrophy are mutually exclusive processes. depending on the age of the organism and the type of tissue, one of these two growth processes dominates.

Taber „Biomechanics of growth, remodeling and morphogenesis" [1995]

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growth, remodeling and morphogenesis

remodeling [riˈmɑd. l.ɪng] involves changes in material properties. These changes, which often are adaptive, may be brought about by alterations in modulus, internal structure, strength, or density. for example, bones, and heart muscle may change their internal structures through reorientation of trabeculae and muscle fibers, respectively.

Taber „Biomechanics of growth, remodeling and morphogenesis" [1995]

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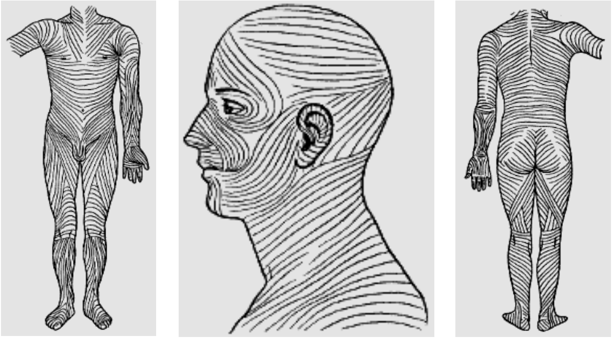
growth, remodeling and morphogenesis

morphogenesis [mɔːr.foˈdʒen.ə.sɪs] is the generation of animal form. usually, the term refers to embryonic development, but wound healing and organ regeneration are also morphogenetic events. morphogenesis contains a complex series of stages, each of which depends on the previous stage. during these stages, genetic and environmental factors guide the spatial-temporal motions and differentiation (specification) of cells. a flaw in any one stage may lead to structural defects.

Taber „Biomechanics of growth, remodeling and morphogenesis" [1995]

langer's lines - anisotropy of human skin



lines of tension - orientation of collagen fiber bundles

Carl Ritter von Langer [1819-1887]

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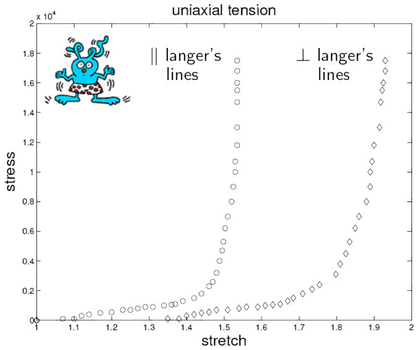
langer's lines - anisotropy of rabbit skin



stiffer || to langer's lines - stress locking @crit stretch

Lanir & Fung [1974]

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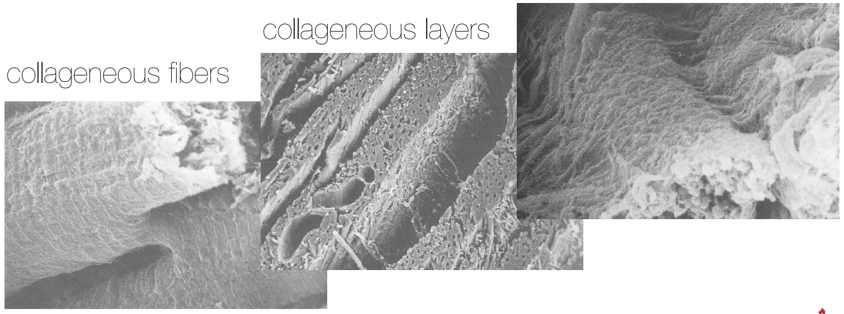
collagen fibers - anisotropy of human tissue



collageneous microstructure

collageneous layers

collageneous fibers

directional strengthening due to collagen fibers

Humphrey [2002]

---

collagen fibers - anisotropy of human tissue

collagen fibrils in tendon

collagen fibrils in skin

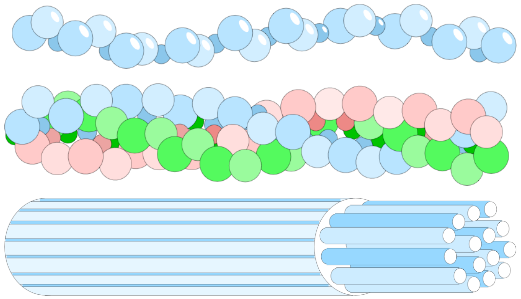
collagen fibrils in skin

directional strengthening due to collagen fibers

Viidik [1973]

collagen fibers - hierarchical microstructure

● glycin ● hydroxyprolin ● prolin amino acids



about 1000 amino acids form collagen α chain

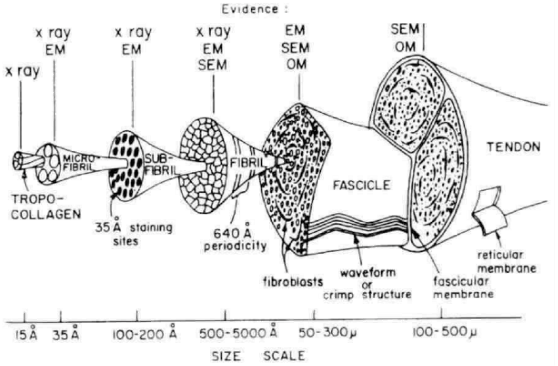
three α chains form collagen triple helix

collagen fibrils form collagen fiber

directional strengthening due to collagen fibers

---

fundamental idea - hierarchical model



limited set of parameters - clear physical interpretation

Galeski & Baer [1978]

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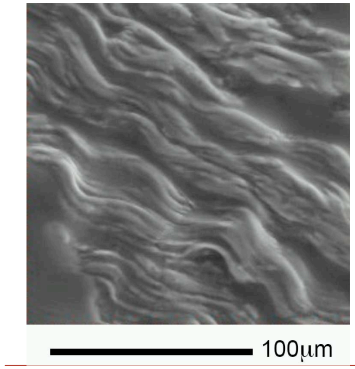
fundamental idea - hierarchical model



hypotheses

I biological tissues seek to restore stress @homeostatic value

II collagen fibers as main load carrying constituents adapt orientation to minimize stress

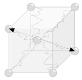
III collagen fiber remodeling can be modeled phenomenologically to provide further insight into tissue's microstructure

collagen fibers in adventitia of human aorta

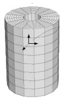
Holzapfel [2005]

I micromechanics • collagen chain

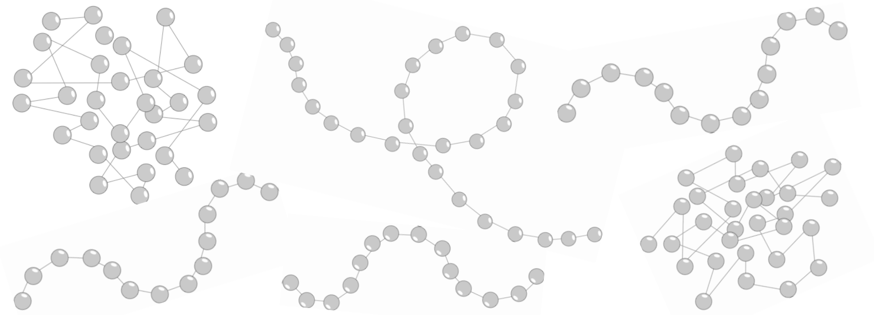
II macromechanics • chain network



III biomechanics • tissue remodeling



statistical mechanics of long chain molecules



entropic elasticity - entropy increases upon stretching

Kuhn [1936], [1938], Porod [1949], Kratky & Porod [1949], Treolar [1958], Flory [1969], Bustamante, Smith, Marko & Siggia [1994], Marko & Siggia [1995], Rief [1997], Holzapfel [2000], Bischoff, Arruda & Grosh [2000], [2002], Ogden, Saccomandi & Sgura [2006]

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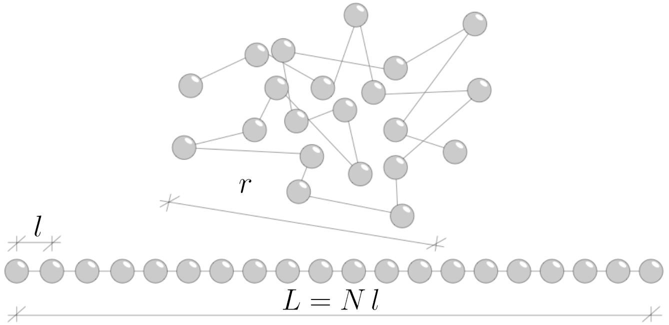
uncorrelated freely jointed chain

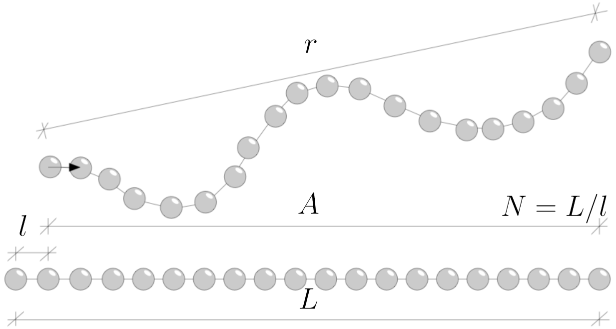


$$\psi^{\text{fjc}} = k\,\theta\,N\left[\frac{r}{\boldsymbol{L}}\mathcal{L}^{-1} + \ln\left(\frac{\mathcal{L}^{-1}}{\sinh(\mathcal{L}^{-1})}\right)\right]$$

micromechanically motivated parameter - contour length $\boldsymbol{L}$

---

correlated wormlike chain



$$\psi^{\text{wlc}} = \frac{k\,\theta\,\boldsymbol{L}}{4\,\boldsymbol{A}}\left[2\,\frac{r^2}{\boldsymbol{L}^2} + \frac{1}{[1 - r/\boldsymbol{L}]} - \frac{r}{\boldsymbol{L}}\right]$$

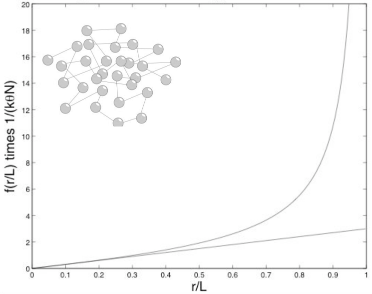
micromechanically motivated parameters - contour length $\boldsymbol{L}$ and persistence length $\boldsymbol{A}$

---

constitutive equations - collagen chain

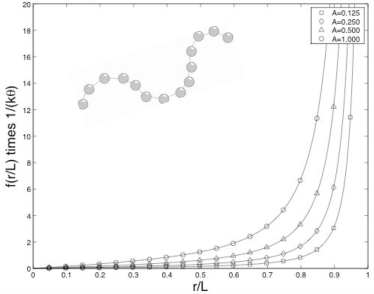
$$f^{\text{fjc}} = k\,\theta\,N\mathcal{L}^{-1}(\tfrac{r}{L})$$

single chain force f – freely jointed chain model



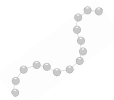
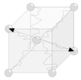
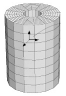
$$f^{\text{wlc}} = \frac{k\,\theta}{4\,A}\left[\frac{4\,r}{L} + \frac{1}{[1-r/L]^2} - 1\right]$$

single chain force f – worm like chain model



characteristic locking behavior - initial stiffness of wlc

micromechanically motivated parameters - contour length $\boldsymbol{L}$ and persistence length $\boldsymbol{A}$

I micromechanics	• collagen chain	
II macromechanics	• chain network	
III biomechanics	• tissue remodeling	

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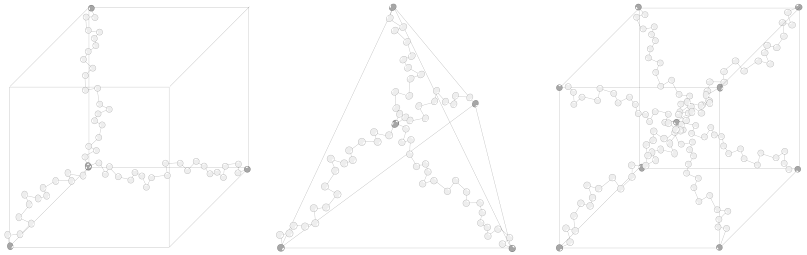
concept of chain network models


three chain model
four chain model
eight chain model

representative isotropic network of cross-linked chains

Flory & Rehner [1943], James & Guth [1943], Wang & Guth [1952], Treloar [1958], Arruda & Boyce [1993], Wu & van der Giessen [1993], Boyce [1996], Boyce & Arruda [2000], Bischoff, Arruda & Grosh [2002], Miehe, Göktepe & Lulei [2004]

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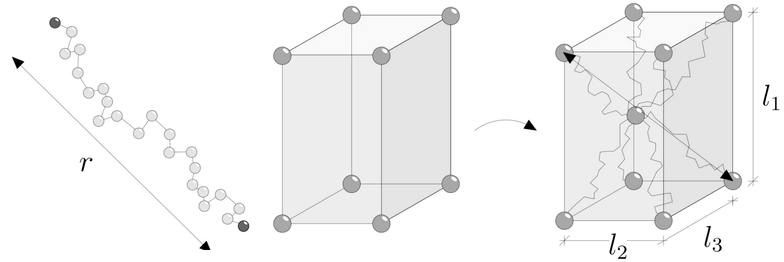
constitutive equations - chain network


eight single chains
isotropic cell matrix
eight chain model

$$\Psi^{\text{chn}} = \tfrac{1}{8}\,\gamma^{\text{chn}} \textstyle\sum_{i=1}^{8} \psi^{\text{wlc}}(r) \qquad \text{with} \qquad r = r(\boldsymbol{F})$$

$$\Psi^{\text{iso}} = \tfrac{1}{2}\,\lambda \ln^2(\det(\boldsymbol{F})) + \tfrac{1}{2}\,\mu[\,\boldsymbol{F}^{\text{t}} : \boldsymbol{F} - n^{\text{dim}} - 2\,\ln(\det(\boldsymbol{F}))\,]$$

micromechanically motivated parameters - chain density γ^{chn} and cell dimensions l_1, l_2, l_3

---

orthotropic chain network model

- general case orthotropic network model

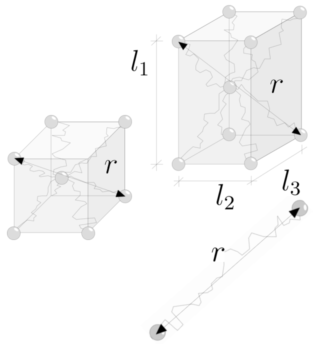
  $l_1 \neq l_2 \neq l_3 \qquad r = \sqrt{l_I^2\, \bar{I}_I^C}$

- special case isotropic network model

  $l_1 = l_2 = l_3 = l \qquad r = l\,\sqrt{I_1^C}$

- special case transversely isotropic model

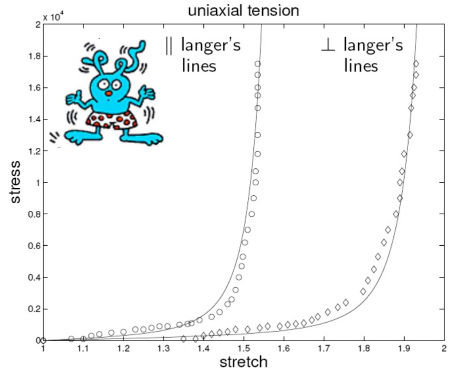
  $l_2 = l_3 = 0 \qquad r = l_1\sqrt{\bar{I}_1^C}$



traditional arruda boyce model as special case

invariants $I_1^C = \boldsymbol{C} : \boldsymbol{I}$ and $\bar{I}_I^C = \boldsymbol{n}_I \cdot \boldsymbol{C} \cdot \boldsymbol{n}_I$

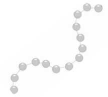
experiment vs simulation - rabbit skin



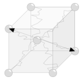
stiffer || to langer's lines - stress locking @crit stretch

Lanir & Fung [1974], Kuhl, Garikipati, Arruda & Grosh [2005]

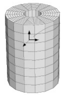
I micromechanics • collagen chain



II macromechanics • chain network



III biomechanics • tissue remodeling



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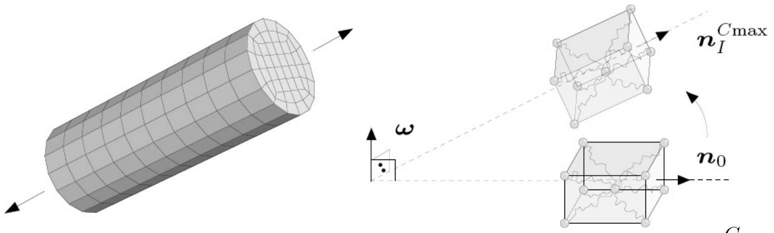
adaptation of microstructural direction



- gradual alignment of fiber direction $\boldsymbol{n}_0$ with max principal strain $\boldsymbol{n}_I^{C\max}$

$$\boldsymbol{n}_0 \rightarrow \boldsymbol{n}_I^{C\max} \qquad \boldsymbol{C} = \lambda_I^C \, \boldsymbol{n}_I^C \otimes \boldsymbol{n}_I^C$$

- exponential update/euler-rodrigues for direction of transverse isotropy $\boldsymbol{n}_0$

$$\boldsymbol{n}_0^{k+1} = \exp(-\Delta t \overset{3}{\boldsymbol{e}} \cdot \boldsymbol{\omega}) \cdot \boldsymbol{n}_0^k \qquad \boldsymbol{\omega} = [\, \boldsymbol{n}_0^k \times \boldsymbol{n}_I^{C\max} \,] \, / \, \kappa_\omega$$

Fyrhie & Carter [1986], Cowin [1989}, [1994], Vianello [1996], Sgarra & Vianello [1997], Menzel [2004], Driessen [2006], Kuhl, Menzel & Garikipati [2006]

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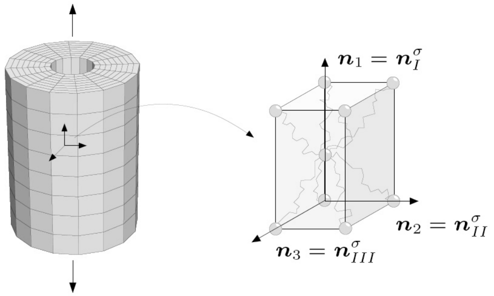
adaptation of microstructural axes

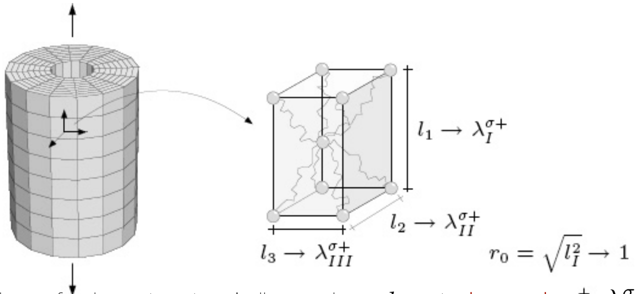


- instantaneous alignment of microstructure $\boldsymbol{n}_I$ wrt eigenvectors $\boldsymbol{n}_I^\sigma$

$$\boldsymbol{n}_I \doteq \boldsymbol{n}_I^\sigma \qquad \boldsymbol{\sigma} = \lambda_I^\sigma \, \boldsymbol{n}_I^\sigma \otimes \boldsymbol{n}_I^\sigma$$

„the unit cell used in each of the network models is taken to deform in principal stretch space." Boyce & Arruda [2000]

adaptation of fiber dimensions



- gradual adaptation of microstructural dimensions l_I wrt eigenvalues $\lambda_I^{\sigma+}$

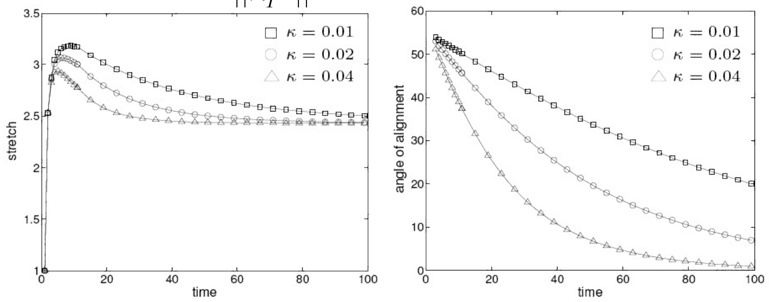
$$l_I \rightarrow \begin{array}{ll} \lambda_I^{\sigma+}/||\lambda_I^{\sigma+}|| & \text{if} \quad \lambda_I^\sigma > 0 \\ 0 & \text{if} \quad \lambda_I^\sigma \leq 0 \end{array} \qquad \boldsymbol{\sigma} = \lambda_I^\sigma \, \boldsymbol{n}_I^\sigma \otimes \boldsymbol{n}_I^\sigma$$

„the collagen fibers are located between the directions of the maximum principal stresses." Hariton, de Botton, Gasser & Holzapfel [2006]

---

remodeling of collagen fibers - uniaxial tension

$$l_I = [\,\frac{\lambda_I^{\sigma+}}{||\lambda_I^{\sigma+}||} - l_I^0\,]\,[\,1 - \exp(-\boldsymbol{\kappa}\,t)\,] + l_I^0$$



stress driven adaptation of microstructure

micromechanically motivated parameter κ

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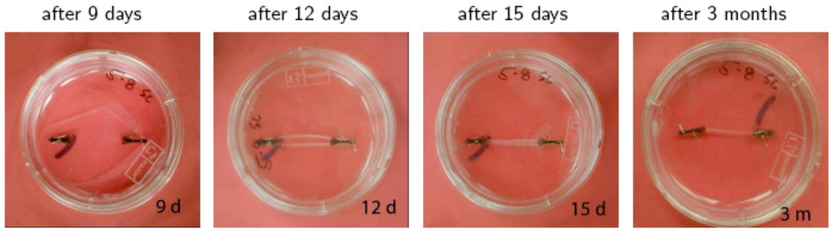
remodeling of collagen fibers - living tendon



- ex vivo engineered tendon shows characteristcs of embryonic tendon
- remodeling of collagen fibers upon mechanical loading
- long term goal mechanically stimulated tissue engineering

Calve, Dennis, Kosnik, Baar, Grosh & Arruda [2004]

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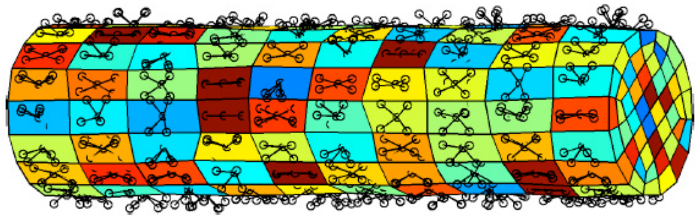
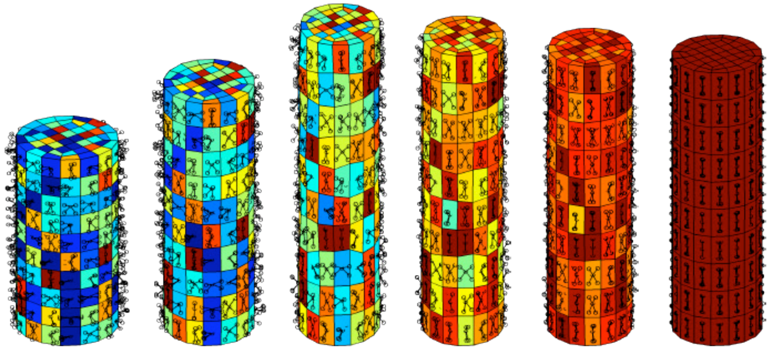
remodeling of collagen fibers - living tendon



- finite element simulation of functional adaptation in tendons
- wormlike chain model with initial random anisotropy
- analysis of fiber reorientation in uniaxial tension

Kuhl, Garikipati, Arruda & Grosh [2005]

remodeling of collagen fibers - living tendon



gradual fiber alignment with max principal stress

example - tissue engineering

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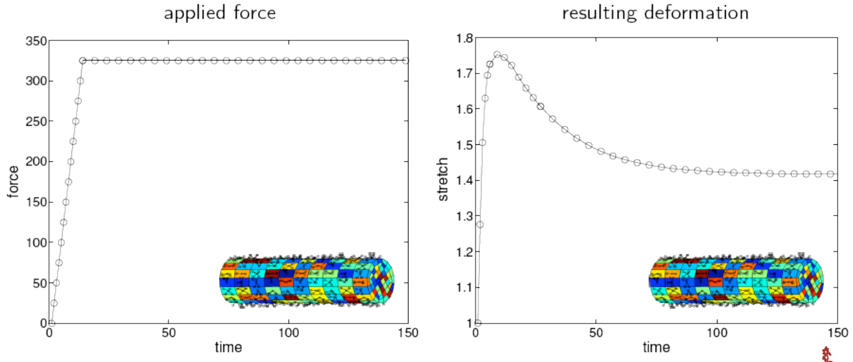
remodeling of collagen fibers - living tendon



characteristic locking, remodeling & stiffening

example - tissue engineering

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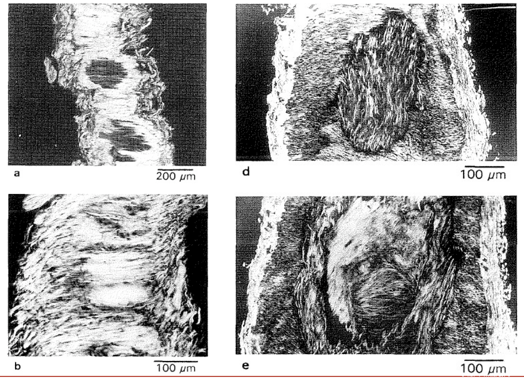
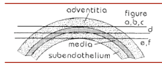
tangentially sectioned brain arteries





circularly polarized light micrographs

Finlay [1995]

example - arterial wall

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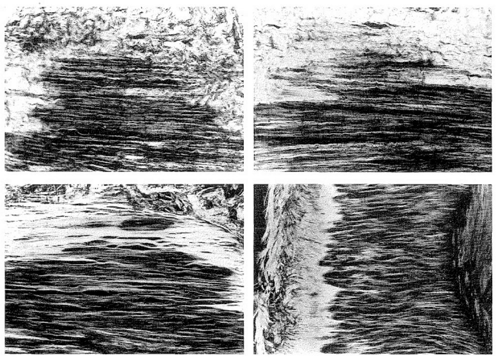
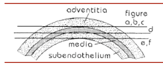
tangentially sectioned brain arteries



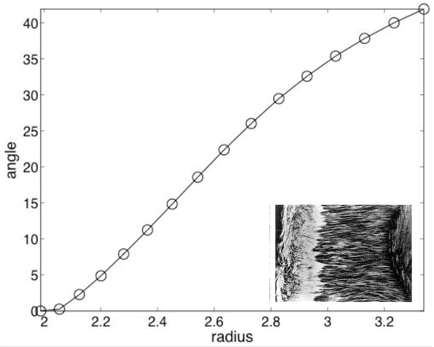


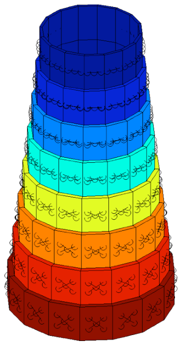
circularly polarized light micrographs

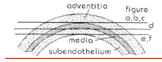
Finlay [1995]

example - arterial wall

remodeling of collagen fibers







stress driven functional adaptation

Kuhl & Holzapfel [2007]

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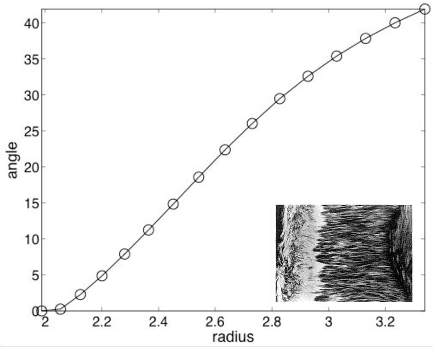
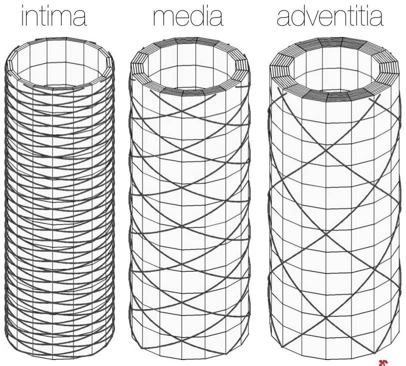
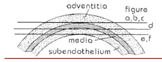
remodeling of collagen fibers







stress driven functional adaptation

Kuhl & Holzapfel [2007]

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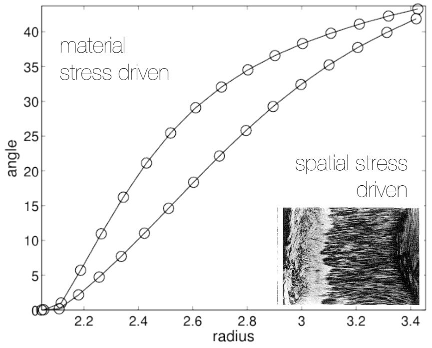
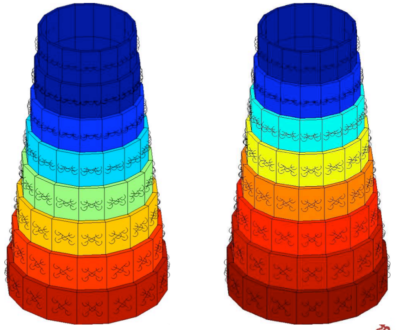
sensitivity wrt driving force - spatial vs material stress



$\boldsymbol{\sigma} = \lambda_I^\sigma \, \boldsymbol{n}_I^\sigma \otimes \boldsymbol{n}_I^\sigma$ $\quad$ $\boldsymbol{S} = \lambda_I^S \, \boldsymbol{n}_I^S \otimes \boldsymbol{n}_I^S$



true spatial driving force more reasonable

Kuhl & Holzapfel [2007]

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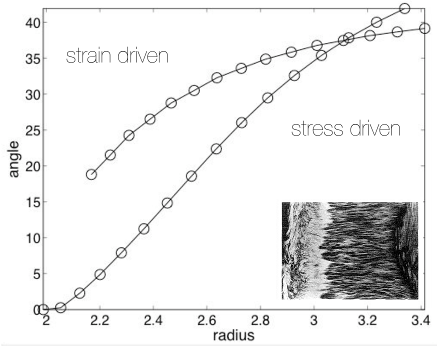
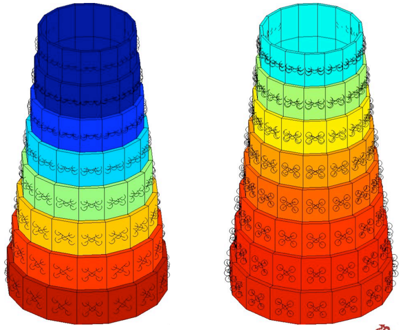
sensitivity wrt driving force - stress vs strain



$\boldsymbol{\sigma} = \lambda_I^\sigma \, \boldsymbol{n}_I^\sigma \otimes \boldsymbol{n}_I^\sigma$ $\quad$ $\boldsymbol{b} = \lambda_I^b \, \boldsymbol{n}_I^b \otimes \boldsymbol{n}_I^b$



eigenvectors coincide but eigenvalues differ significantly

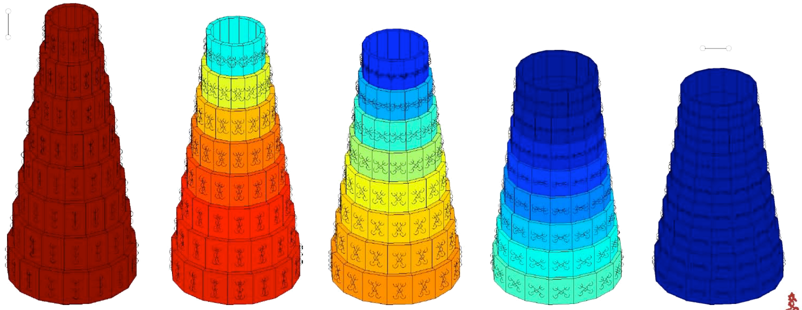
Kuhl & Holzapfel [2007]

sensitivity wrt pressure to stretch ratio

$\epsilon_{zz} = 10\%$
$p = 0$

<< increase of stretch <<
>> increase of pressure >>

$\epsilon_{zz} = 0\%$
$p = p^{\text{blood}}$



collagen fiber angle governed by pressure2stretch ratio

Kuhl & Holzapfel [2007]

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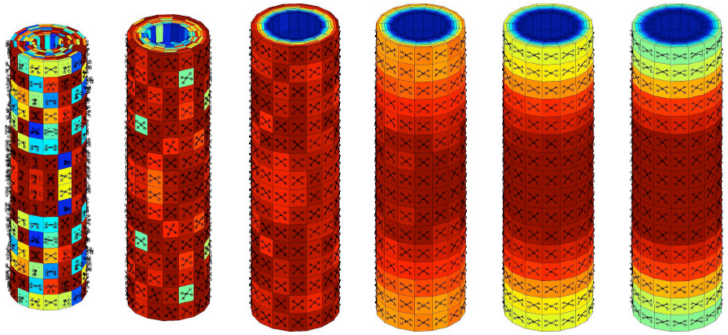
sensitivity wrt changes in mechanical loading

>> axial strain and blood pressure >>

>> local increase of pressure >>



fiber reorientation in response to changes in loading

Kuhl & Holzapfel [2007]

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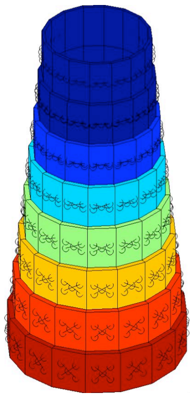
hierarchical continuum model for living tissues



- fully three dimensional

  orthotropy • transverse isotropy • isotropy
- micromechanically motivated

  limited set of parameters $\lambda, \mu, L, A, \gamma^{\text{chn}}$
- non-affine chain network

  $\boldsymbol{n}_I$ adapt instantaneously wrt eigenvectors $\boldsymbol{n}_I \doteq \boldsymbol{n}_I^{\sigma}$

  l_I adapt gradually wrt eigenvalues $l_I \rightarrow \lambda_I^{\sigma^+} / ||\lambda_I^{\sigma^+}||$
- stress vs strain driven remodeling

  eigenvectors commute • eigenvalues do not

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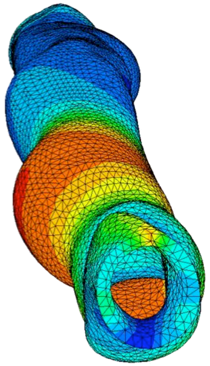
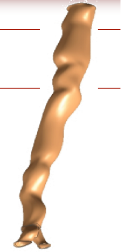
challenges - mechanotransduction





- how do tissues sense mechanical stimuli?

  receptors on cell surface • cytoskeleton
- how are signals transmitted?

  focal adhesion • role of biochemistry • ion channels
- how does remodeling take place?

  collagen synthesis / turnover • gene expression

mechanics of the cell