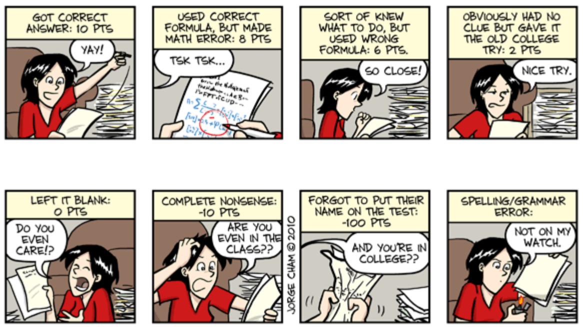
18 – remodeling
fiber reorientation

day	date		topic
tue	jan	10	motivation - everything grows!
thu	jan	12	basics maths - notation and tensors
tue	jan	17	basic kinematics - large deformation and growth
thu	jan	19	kinematics - growing hearts
tue	jan	24	guest lecture - growing skin
thu	jan	26	guest lecture - growing leaflets
tue	jan	31	basic balance equations - closed and open systems
thu	feb	02	basic constitutive equations - growing tumors
tue	feb	07	volume growth - finite elements for growth
thu	feb	09	volume growth - growing arteries
tue	feb	14	volume growth - growing skin
thu	feb	16	volume growth - growing hearts
tue	feb	21	basic constitutive equations - growing bones
thu	feb	23	density growth - finite elements for growth
tue	feb	28	density growth - growing bones
thu	mar	01	everything grows! - midterm summary
tue	mar	06	midterm
thu	mar	08	remodeling - remodeling arteries and tendons
tue	mar	13	class project - discussion, presentation, evaluation
thu	mar	15	class project - discussion, presentation, evaluation
thu	mar	15	written part of final projects due

me 337 - grading



- 30 % homework - 3 homework assignments, 10% each
- 30 % midterm - closed book, closed notes, one single page cheat sheet
- 20 % final project oral presentations - graded by the class
- 20 % final project essay - graded by instructor

final projects

- **tendon growth**: harrison, brandon, mohammed, matthew
- **tendon growth and remodeling**: peter & jina
- **muscle growth**: alex
- **wound healing**: beth, ann, armen
- **benign vocal fold nodule and polyp growth**: corey
- **growth of swelling gels**: hardik, xi
- **bone growth**: kevin, alison, safwan, kamil

ME 337 – Mechanics of Growth

Final Project Presentations

Instructions for Judges
according to ASME / SBC conference review guidelines

The presentation format includes the **structure of the presentaiton and its composition**. In general, a presentation should be structured to include an introduction, method, analysis, results, a conclusion, and references. The introduction should define the problem, scope of the study, and a brief background of previous work. The method section also should be brief to leave the majority of the report body for results and discussion. The final paragraph should be a brief paragraph on inference or conclusions reached.

Technical merit should be judged on the completeness of what is reported. For scientific studies, the result should support the conclusions presented. The key is validation of the express conclusion with results and data. Unsubstantiated conclusions or results should receive minimum points. However, not all papers represent basic research. Some papers present the design of a hardware system or a new software development. Both require the development of tests and measurement procedures to validate the product.

After the scoring is complete, please indicate a final grade. Please provide a comment in the designated area that describes why you think this presentation suitable/not suitable. These comments will be collected and provide to the students for feedback.

almost done…

ME 337 – Mechanics of Growth

Is not necessary for the judge to be an expert in the field represented by the paper to evaluate its technical merit using these criteria. Subjective rating of the paper's scientific contribution is not encouraged unless there is evidence that the conclusions are incorrect. A judge should feel free to consult colleagues who are experts in the field, if you are unsure about the correctness of the conclusions. Since presentations can vary from hardware designs to software technique, or simulations and modeling to basic research, each reviewer will have to use his/her own best judgment about the technical merit of the work that is presented.

Scoring & Evaluation System:

Please use the same scoring system as for the General Abstracts for each of the evaluation categories.

Score – Provide a ranking according to

Excellent	= 100
Very Good	= 90
Good	= 80
Marginal	= 60
Poor	= 50

Evaluation Categories

1. Structure of presentation
2. Technical merit
3. Style of presentation

groups & dates…

Keep in mind the judges cannot be perfect, but will try to be consistent in scoring. There are multiple judges for

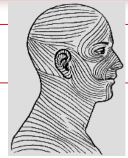
almost done…

growth, remodeling and morphogenesis

remodeling [riˈmɑd. l.ɪŋ] 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]

remodeling



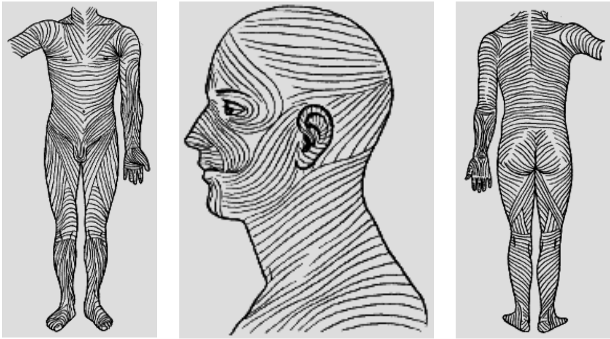
langer's lines - anisotropy of human skin

langer's lines, sometimes called cleavage lines, are topological lines drawn on a map of the human body. they are defined by the direction in which the human skin would split when struck with a spike. langer's lines correspond to the natural orientation of collagen fibers in the dermis and epidermis. knowing the direction of langer's lines within a specific area of the skin is important for surgical procedures. particularly cosmetic surgery involving the skin. if a surgeon has a choice about where and in what direction to place an incision, he may choose to cut in the direction of langer's lines. incisions made parallel to langer's lines may heal better and produce less scarring than those cut across.

Wikipedia The Free Encyclopedia

remodeling - motivation

langer's lines - anisotropy of human skin

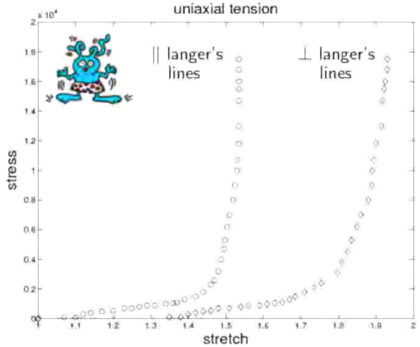


lines of tension - orientation of collagen fiber bundles

carl ritter von langer [1819-1887]

remodeling - motivation

langer's lines - anisotropy of rabbit skin



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

lanir & fung [1974]

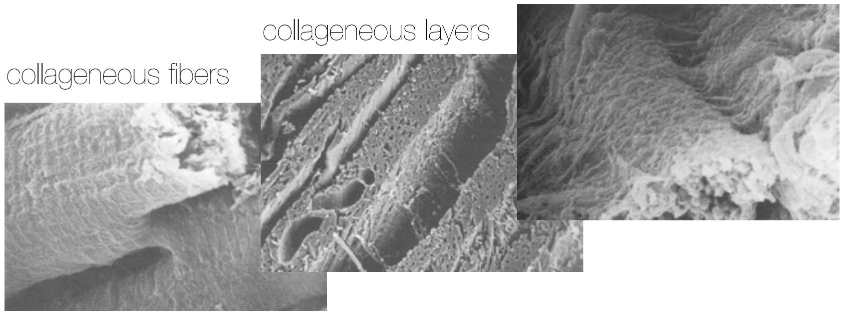
remodeling - motivation

collagen fibers - anisotropy of human tissue

collageneous microstructure

collageneous layers

collageneous fibers



directional strengthening due to collagen fibers

humphrey [2002]

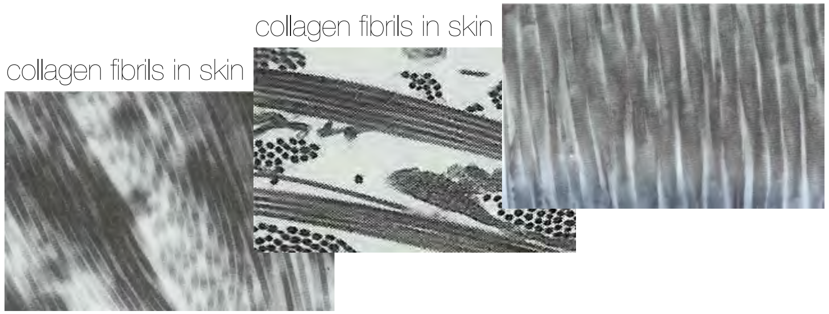
remodeling - motivation

collagen fibers - anisotropy of human tissue

collagen fibrils in tendon

collagen fibrils in skin

collagen fibrils in skin



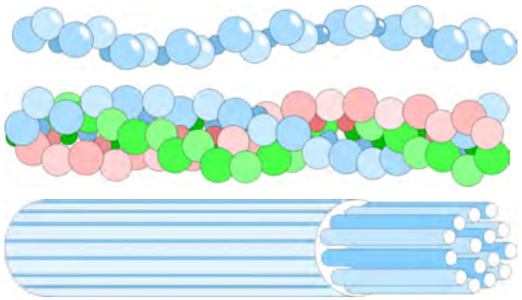
directional strengthening due to collagen fibers

viidik [1973]

remodeling - motivation

collagen fibers - hierarchical microstructure

glycin hydroxyprolin prolin amino acids



about 1000 amino acids form collagen α chain

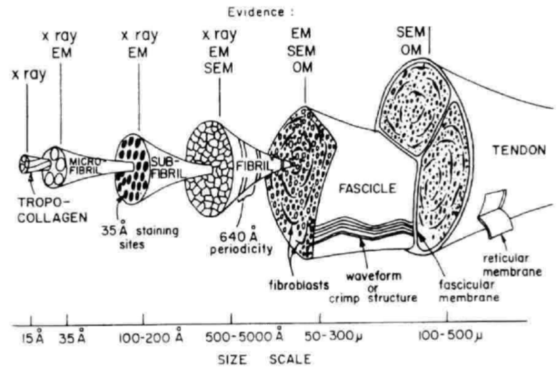
three α chains form collagen triple helix

collagen fibrils form collagen fiber

directional strengthening due to collagen fibers

remodeling - motivation 13

fundamental idea - hierarchical modelling

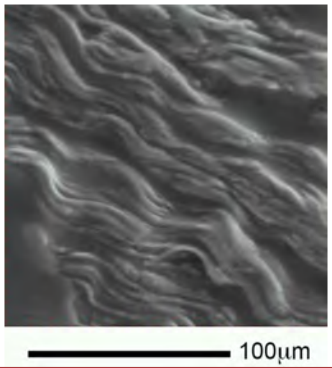


limited set of parameters - clear physical interpretation

galeski & baer [1978]

remodeling - motivation 14

fundamental idea - hierarchical modelling



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]

remodeling - motivation 15

I micromechanics • collagen chain

II macromechanics • chain network

III biomechanics • tissue remodeling

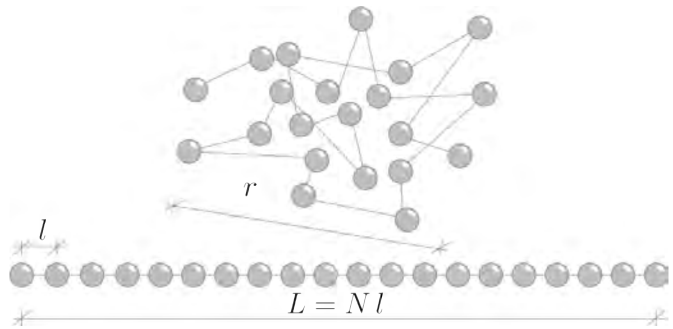
remodeling - micromechanics 16

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]

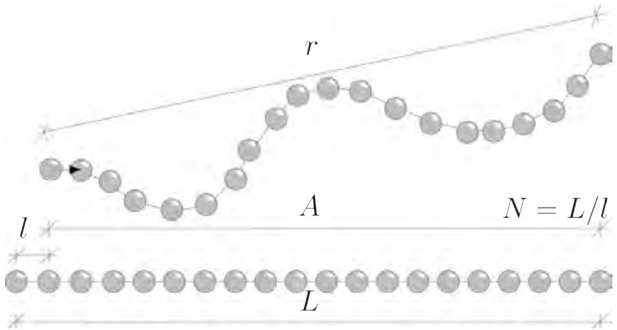
uncorrelated freely jointed chain



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

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

correlated wormlike chain

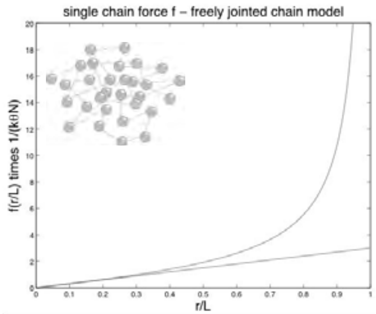


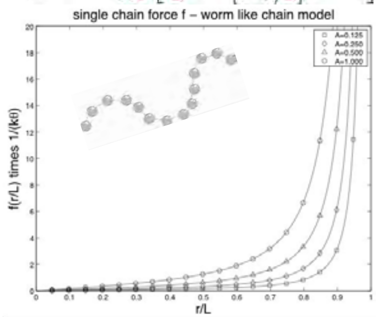
$$\psi^{\text{wlc}} = \frac{k\,\theta\,\boldsymbol{L}}{4\,\boldsymbol{A}}\left[2\,\frac{r^2}{\boldsymbol{L}^2} + \frac{1}{[1 - r/\boldsymbol{L}]} - \frac{r}{\boldsymbol{L}}\right]$$

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

constitutive equations - collagen chain

$$f^{\text{fjc}} = k\,\theta\,N\mathcal{L}^{-1}\left(\tfrac{r}{\boldsymbol{L}}\right) \qquad f^{\text{wlc}} = \frac{k\,\theta}{4\,\boldsymbol{A}}\left[\frac{4\,r}{\boldsymbol{L}} + \frac{1}{[1-r/\boldsymbol{L}]^2} - 1\right]$$





characteristic locking behavior - initial stiffness of wlc

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

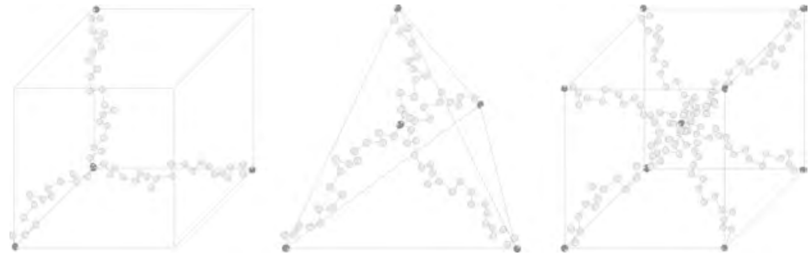
I micromechanics • collagen chain 

II macromechanics • chain network 

III biomechanics • tissue remodeling 

chain network models

three chain model | four chain model | eight chain model

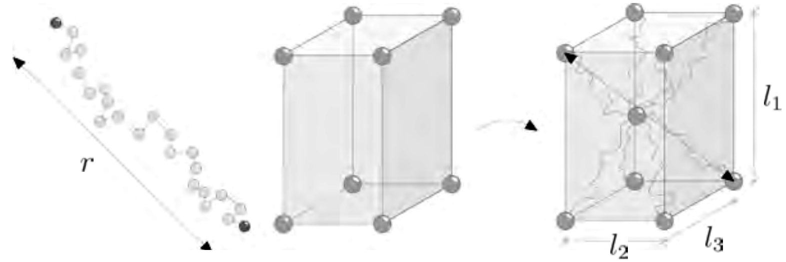


representative isotropic network of cross-linked chains

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]

constitutive equations - chain network

eight single chains | isotropic cell matrix | eight chain model



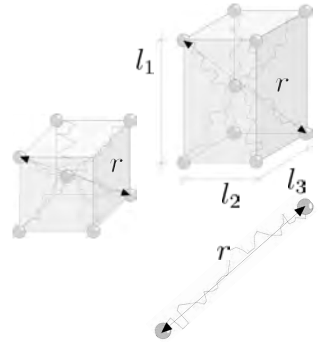
$\Psi^{\text{chn}} = \frac{1}{8}\,\gamma^{\text{chn}} \sum_{i=1}^{8} \psi^{\text{wlc}}(r)$ with $r = r(\boldsymbol{F})$

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

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

orthotropic chain network model

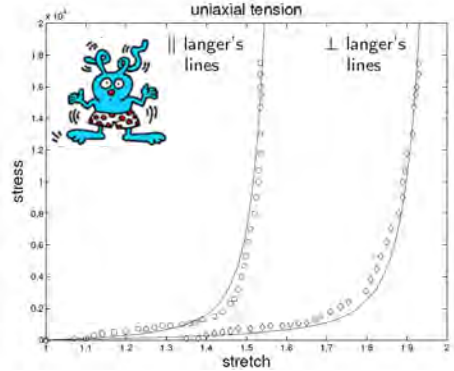
- general case orthotropic network model
  $l_1 \neq l_2 \neq l_3$ $\quad r = \sqrt{l_I^2\,\bar{I}_I^C}$
- special case isotropic network model
  $l_1 = l_2 = l_3 = l$ $\quad r = l\,\sqrt{I_1^C}$
- special case transversely isotropic model
  $l_2 = l_3 = 0$ $\quad r = l_1\sqrt{\bar{I}_1^C}$



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 

adaptation of microstructural direction

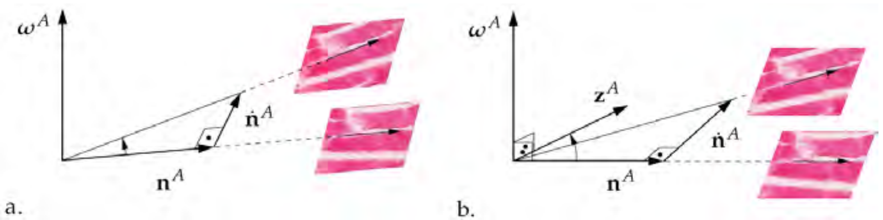
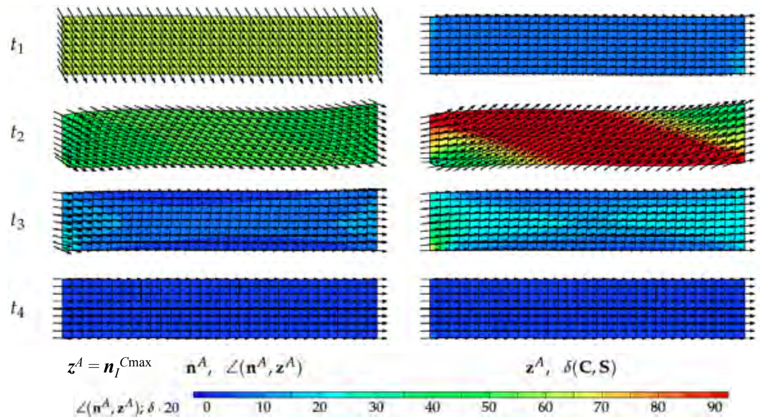


figure 5.1. the characteristic direction $\boldsymbol{n}^A$ rotates such that, in the equilibrium state, it is aligned with the target direction $\boldsymbol{z}^A$. to avoid drilling rotation, the angular velocity $\boldsymbol{\omega}^A$ must be perpendicular to the plane spanned by the vectors $\boldsymbol{n}^A$ and $\boldsymbol{z}^A$. the change in direction $D_t\, \boldsymbol{n}^A$ can then be expressed as $D_t\, \boldsymbol{n}^A = \boldsymbol{\omega}^A \times \boldsymbol{n}^A$. the target direction $\boldsymbol{z}^A$ could, for example, be the maximum principal strain $\boldsymbol{n}_I^{Cmax}$ or the maximum principal stress $\boldsymbol{n}_I^{Smax}$.

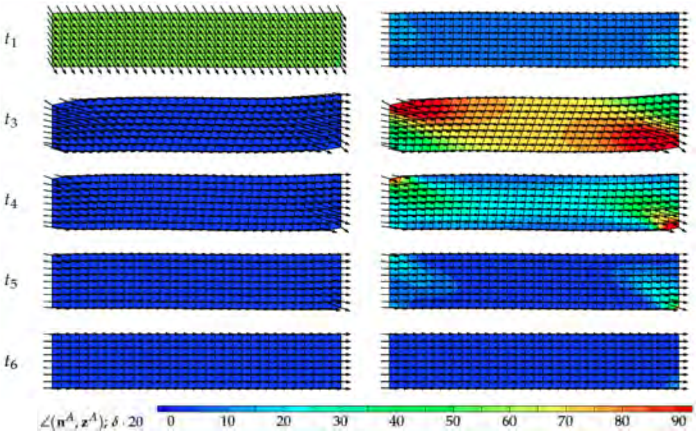
himpel [2007], himpel, menzel, kuhl & steinmann [2008]

strain-driven adaptation of microstructural direction



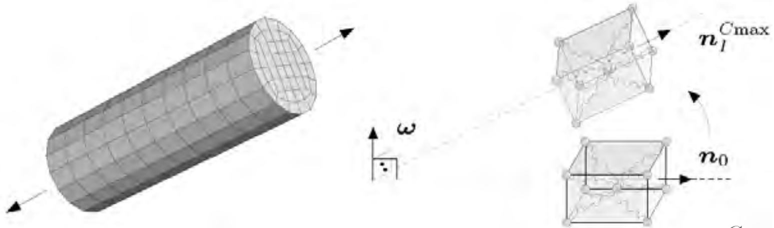
himpel [2007], himpel, menzel, kuhl & steinmann [2008]

stress-driven adaptation of microstructural direction



himpel [2007], himpel, menzel, kuhl & steinmann [2008]

adaptation of microstructural direction



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

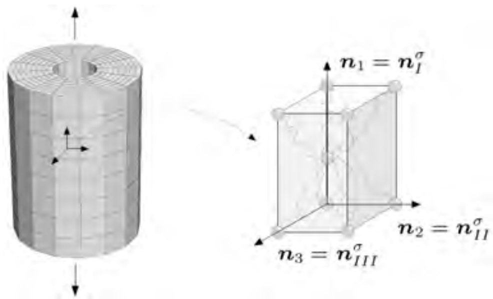
$$\boldsymbol{n}_0 \rightarrow \boldsymbol{n}_I^{C\max} \qquad \boldsymbol{C} = \lambda_I^C \, \boldsymbol{n}_I^C \otimes \boldsymbol{n}_I^C$$

- 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]

adaptation of microstructural axes

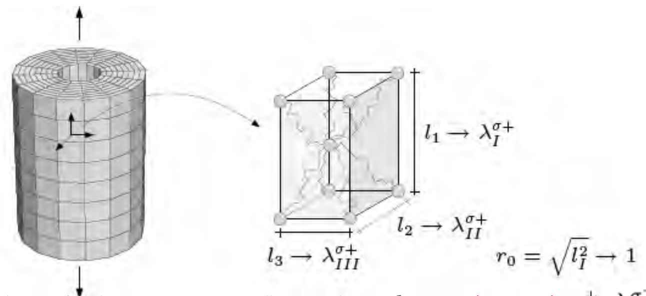


- instantaneous alignment of microstructure $\boldsymbol{n}_I$ wrt eigenvectors $\boldsymbol{n}_I^\sigma$

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

„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



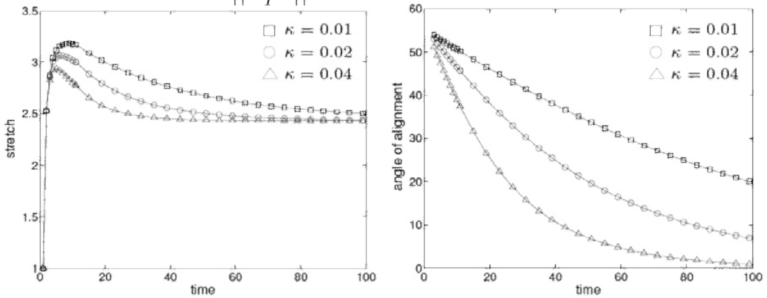
- gradual adaptation of microstructural dimensions l_I wrt eigenvalues $\lambda_I^{\sigma+}$

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

„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

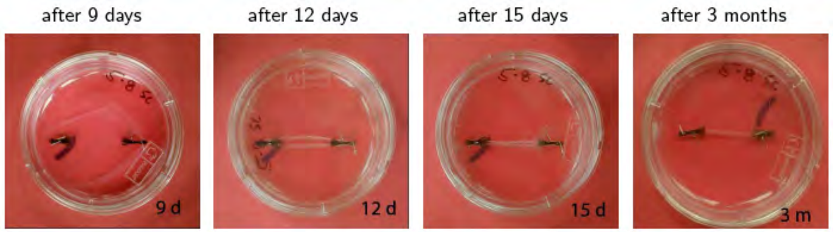
$$l_I = \left[\, \frac{\lambda_I^{\sigma^+}}{||\lambda_I^{\sigma^+}||} - l_I^0 \,\right] [\, 1 - \exp(-\kappa\, t)\,] + l_I^0$$



stress driven adaptation of microstructure

micromechanically motivated parameter κ

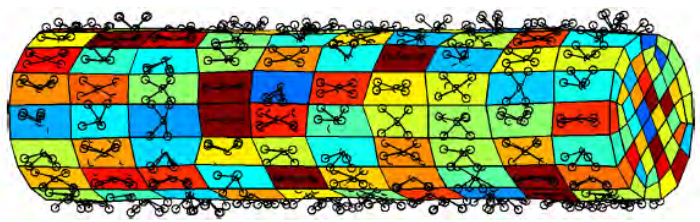
remodeling of collagen fibers - living tendon



- 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]

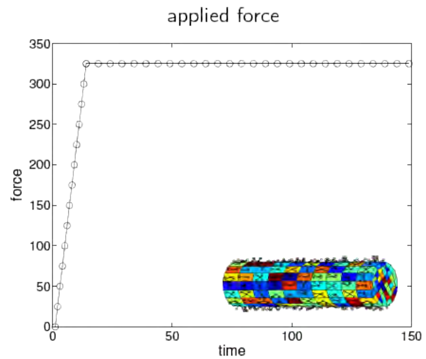
remodeling of collagen fibers - living tendon

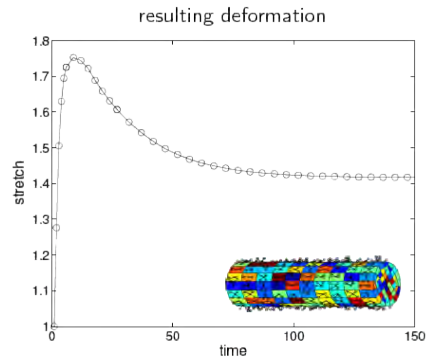


- finite element simulation of functional adaptation in tendons
- wormlike chain model with initial random anisotropy
- analysis of fiber reorientation in uniaxial tension

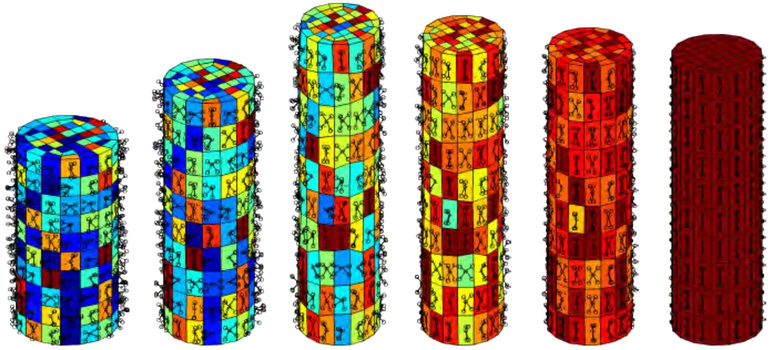
kuhl, garikipati, arruda & grosh [2005]

remodeling of collagen fibers - living tendon





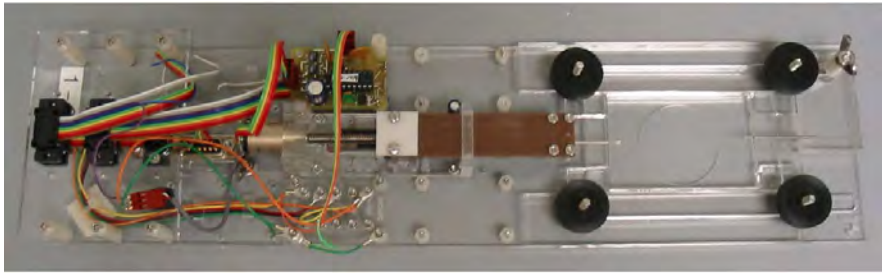
characteristic locking, remodeling & stiffening remodeling of collagen fibers - living tendon



gradual fiber alignment with max principal stress

example - tissue engineering

remodeling of collagen fibers - living tendon

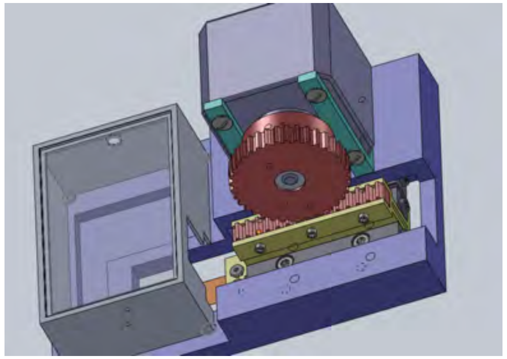


tissue stretcher - cyclic loading
mechanically stimulated reorientation of collagen fibers

courtesy of sarah calve & ellen arruda, mechanical engineering, university of michigan

example - tissue engineering

alignment of cells - iPSC-derived heart muscle cells

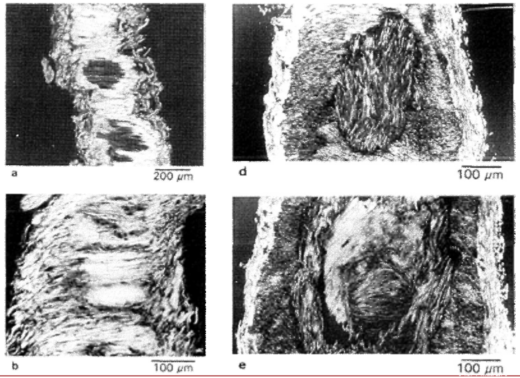


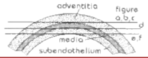
mechanically stimulated stem cell differentiation

courtesy of oscar abilez, bioengineering, stanford university

example - stem cell differentiaton

tangentially sectioned brain arteries



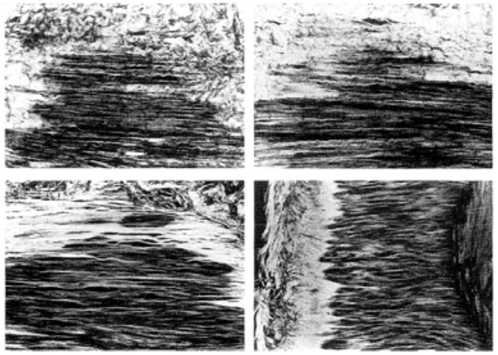


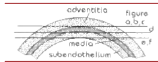
circularly polarized light micrographs

finlay [1995]

example - arterial wall

tangentially sectioned brain arteries

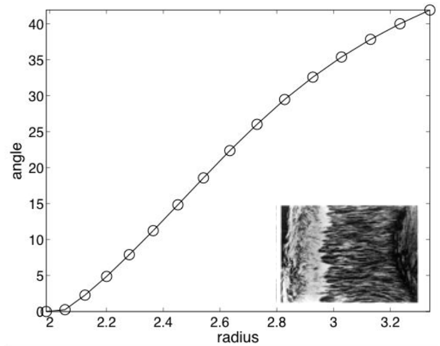


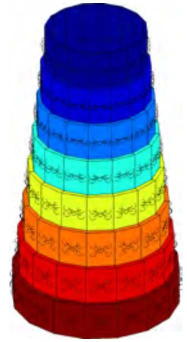


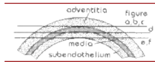
circularly polarized light micrographs

finlay [1995]

remodeling of collagen fibers



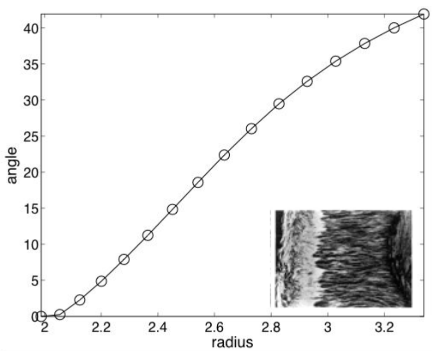


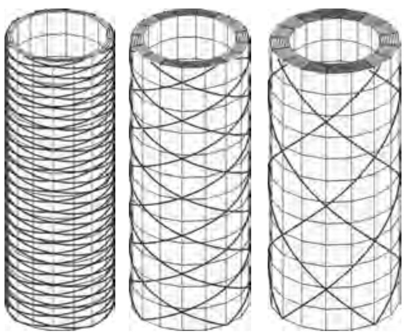


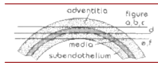
stress driven functional adaptation

kuhl & holzapfel [2007]

remodeling of collagen fibers



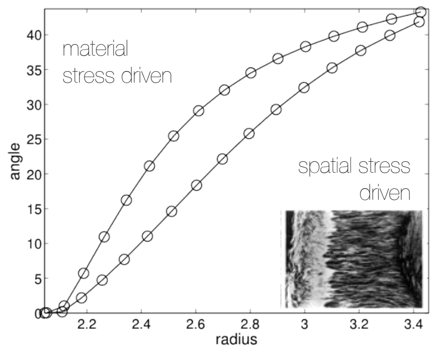




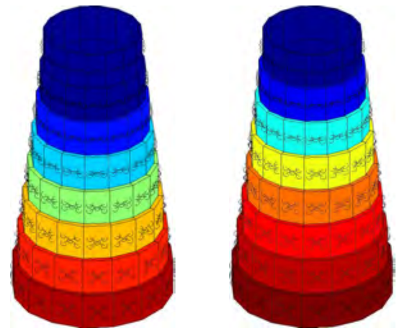
stress driven functional adaptation

kuhl & holzapfel [2007]

sensitivity wrt driving force - spatial vs material stress



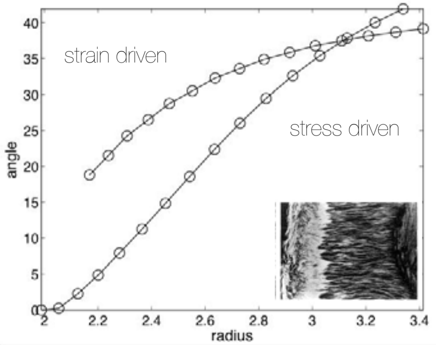
$\boldsymbol{\sigma} = \lambda_I^\sigma \, \boldsymbol{n}_I^\sigma \otimes \boldsymbol{n}_I^\sigma$ $\quad$ $\boldsymbol{S} = \lambda_I^S \, \boldsymbol{n}_I^S \otimes \boldsymbol{n}_I^S$



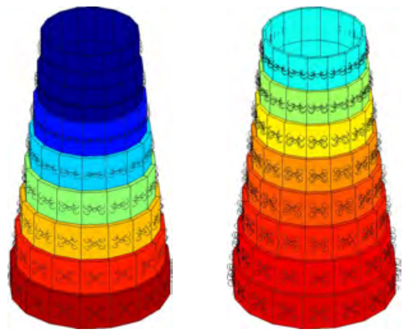
true spatial driving force more reasonable

kuhl & holzapfel [2007]

sensitivity wrt driving force - stress vs strain



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



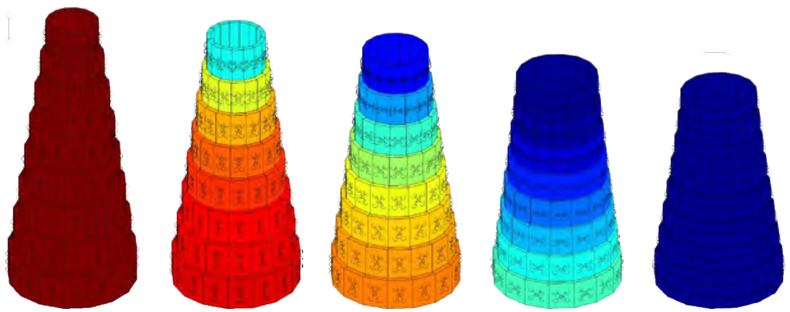
eigenvectors coincide but eigenvalues differ significantly

kuhl & holzapfel [2007]

example - arterial wall

sensitivity wrt pressure to stretch ratio

$\epsilon_{zz} = 10\%$, $p = 0$ — << increase of stretch << / >> increase of pressure >> — $\epsilon_{zz} = 0\%$, $p = p^{\text{blood}}$



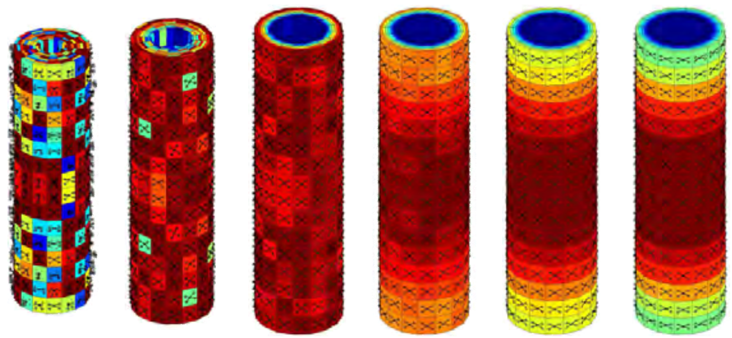
collagen fiber angle governed by pressure2stretch ratio

kuhl & holzapfel [2007]

example - arterial wall

sensitivity wrt changes in mechanical loading

>> axial strain and blood pressure >> >> local increase of pressure >>

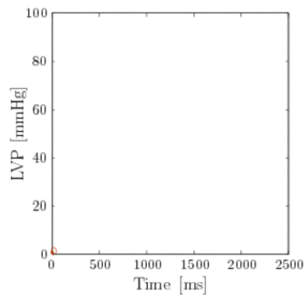


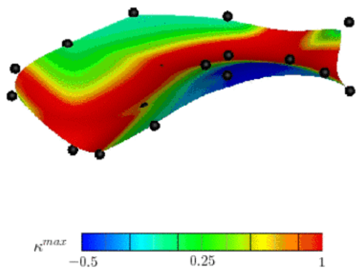
fiber reorientation in response to changes in loading

kuhl & holzapfel [2007]

example - arterial wall

collagen fiber orientation in the mitral valve leaflet



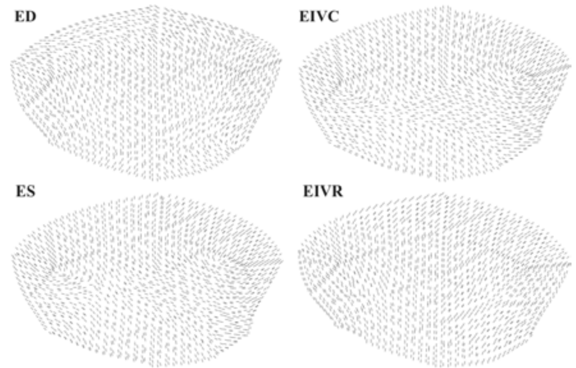


are collagen fibers aligned w/maximum principal strains?

shultz, rausch, kuhl [2010]

example - mitral valve leaflet

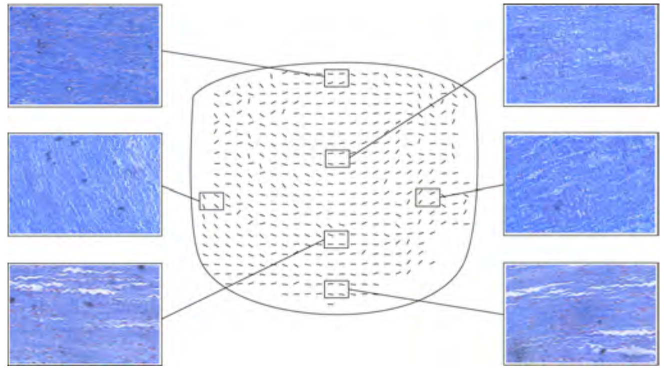
collagen fiber orientation in the mitral valve leaflet



are collagen fibers aligned w/maximum principal strains?

shultz, rausch, kuhl [2010]

collagen fiber orientation in the mitral valve leaflet



are collagen fibers aligned w/maximum principal strains?

shultz, rausch, kuhl [2010]

collagen fiber orientation in the aortic valve leaflet

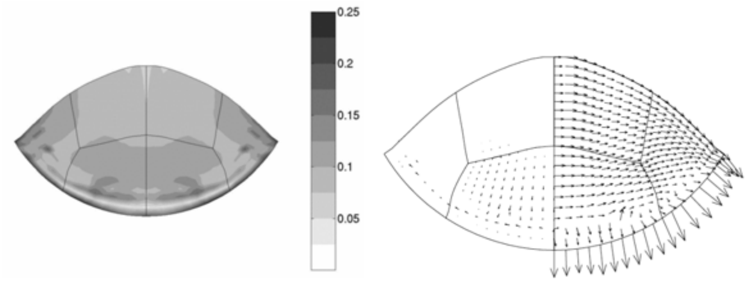
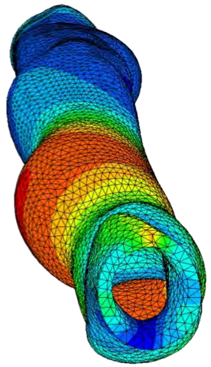


figure 2.6. computationally predicted fiber orientations. mean value of the final total volume fraction on the aortic and ventricular side (left) and final fiber orientation on the aortic sdie of the leaflet (right).

are collagen fibers aligned w/maximum principal strains?

driessen [2006]

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