18 – remodelling
fiber reorientation

ME 337 – Mechanics of Growth

Final Project Presentations
Nov 30 & Dec 02, 2010

Instructions for Judges
according to ASME / SSC conference review guidelines

The presentation format includes the structure of the presentation 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...

18 - remodelling

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

almost done...
almost done...

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.

remodeling - motivation

growth, remodeling and morphogenesis

remodeling [ri’mul.d. limg] 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]

lines of tension - orientation of collagen fiber bundles

carl ritter von langer [1819-1887]
Langer's lines - anisotropy of rabbit skin

Collagen fibers - anisotropy of human tissue

Stiffer \( \parallel \) to Langer's lines - stress locking @ crit stretch

Directional strengthening due to collagen fibers

Remodeling - motivation

Collagen fibers - hierarchical microstructure

- Glycin
- Hydroxyprolin
- Prolin
- Amino acids
- About 1000 amino acids form collagen \( \alpha \) chain
- Three \( \alpha \) chains form collagen triple helix
- Collagen fibrils form collagen fiber

Remodeling - motivation
fundamental idea - hierarchical modelling

limited set of parameters - clear physical interpretation
galeski & baer [1976]

remodeling - motivation

• micromechanics
• macromechanics
• biomechanics

• collagen chain
• chain network
• tissue remodeling

hypotheses
- biological tissues seek to restore stress at homeostatic value
- collagen fibers as main load carrying constituents adapt orientation to minimize stress
- 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

statistical mechanics of long chain molecules

entropic elasticity - entropy increases upon stretching

micromechanically motivated parameter - contour length $L$

remodeling - micromechanics

constitutive equations - collagen chain

$F_{\text{fic}} = k \theta N \left( \frac{r}{L} - \frac{L}{L} \right)$

single chain force $F$ – freely jointed chain model

$F_{\text{wlc}} = \frac{k \theta}{4A} \left( \frac{4r^2}{L^2} + \frac{1}{1-r/L^2} - 1 \right)$

single chain force $F$ – worm like chain model

characteristic locking behavior - initial stiffness of wlc

micromechanically motivated parameters - contour length $L$ and persistence length $A$

remodeling - micromechanics

remodeling - micromechanics

remodeling - micromechanics

remodeling - macromechanics

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


orthotropic chain network model

- general case orthotropic network model
  \[ l_1 \neq l_2 \neq l_3 \quad r = \sqrt{l_1^2 + l_2^2} \]
- special case isotropic network model
  \[ l_1 = l_2 = l_3 = l \quad r = l \sqrt{l_1^2} \]
- special case transversely isotropic model
  \[ l_2 = l_3 = 0 \quad r = l_1 \sqrt{l_1^2} \]

traditional arruda boyce model as special case

invariants \( I_1^C = C : I \) and \( \tilde{I}_i^C = n_i \cdot C \cdot n_i \)

remodeling - macromechanics

constitutive equations - chain network

eight single chains | isotropic cell matrix | eight chain model

\[
\begin{align*}
\Psi^{\text{chn}} &= \frac{1}{8} \gamma^{\text{chn}} \sum_{i=1}^{8} \psi^{\text{we}}(r) \quad \text{with} \quad r = r(F) \\
\Psi^{\text{iso}} &= \frac{1}{2} \lambda \ln^2(\det(F)) + \frac{1}{2} \mu [ F^t : F - n^{\text{dim}} - 2 \ln(\det(F)) ]
\end{align*}
\]

micromechanically motivated parameters - chain density \( \gamma^{\text{chn}} \) and cell dimensions \( l_1, l_2, l_3 \)

remodeling - macromechanics

experiment vs simulation - rabbit skin

stiffer \( | \parallel \text{to langer's lines - stress locking} @ \text{crit stretch} \)

\[ (\text{lanir} \& \text{fung} [1974], \text{kuhl, garikipati, arruda} \& \text{gresh} [2005]) \]

example - rabbit skin
figure 5.1: the characteristic direction \( n^4 \) rotates such that, in the equilibrium state, it is aligned with the target direction \( z^4 \). To avoid drilling rotation, the angular velocity \( \omega^4 \) must be perpendicular to the plane spanned by the vectors \( n^4 \) and \( z^4 \). The change in direction \( D \) can then be expressed as \( D = n^4 \times \omega^4 \). The target direction \( z^4 \) could, for example, be the maximum principal strain \( n^{C, \text{max}}_I \) or the maximum principal stress \( n^{S, \text{max}}_I \).

himpel [2007], himpel, menzel, kuhl & steinmann [2008]
adaptation of microstructural direction

• gradual alignment of fiber direction $\mathbf{n}_0$ with max principal strain $\mathbf{n}_\text{I}^{\text{max}}$

\[ \mathbf{n}_0 \rightarrow \mathbf{n}_\text{I}^{\text{max}} \]

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

\[ \mathbf{n}_0^{k+1} = \exp(-\Delta t \frac{3}{2} \cdot \omega) \cdot \mathbf{n}_0^k \quad \omega = [\mathbf{n}_0^k \times \mathbf{n}_\text{I}^{\text{max}}] / \kappa \omega \]


remodeling - biomechanics

adaptation of fiber dimensions

• gradual adaptation of microstructural dimensions $l_I$ wrt eigenvectors $\lambda_I^+$

\[ l_I \rightarrow \frac{\lambda_I^+}{||\lambda_I^+||} \quad \text{if} \quad \lambda_I^+ > 0 \quad \text{and} \quad l_I \rightarrow 0 \quad \text{if} \quad \lambda_I^+ \leq 0 \]

\[ \mathbf{\sigma} = \lambda_I^+ \mathbf{n}_I^+ \otimes \mathbf{n}_I^+ \]

"the collagen fibers are located between the directions of the maximum principal stresses." hanlon, de botton, gasser & holzapfel [2006]

remodeling - biomechanics

remodeling of collagen fibers - uniaxial tension

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

stress driven adaptation of microstructure

micromechanically motivated parameter $\kappa$
- ex vivo engineered tendon shows characteristics of embryonic tendon
- remodeling of collagen fibers upon mechanical loading
- long term goal mechanically stimulated tissue engineering

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

Example - Tissue Engineering

- 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]
remodelling 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

tangentially sectioned brain arteries

circularly polarized light micrographs

example - arterial wall

alignment of cells - iPSC-derived heart muscle cells

mechanically stimulated stem cell differentiation

courtesy of oscar ablez, bioengineering, stanford university

example - stem cell differentiation

tangentially sectioned brain arteries

circularly polarized light micrographs

example - arterial wall

finlay [1995]
remodeling of collagen fibers

stress driven functional adaptation
kuhl & holzapfel [2007]

example - arterial wall
41

sensitivity wrt driving force - spatial vs material stress

true spatial driving force more reasonable
kuhl & holzapfel [2007]

example - arterial wall
43

remodeling of collagen fibers

stress driven functional adaptation
kuhl & holzapfel [2007]

example - arterial wall
42

sensitivity wrt driving force - stress vs strain

eigenvectors coincide but eigenvalues differ significantly
kuhl & holzapfel [2007]

example - arterial wall
44
sensitivity wrt pressure to stretch ratio

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

$<<$ increase of stretch $<<$

$>>$ increase of pressure $>>$

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

$sensitivity wrt changes in mechanical loading$

$>>$ axial strain and blood pressure $>>$

$>>$ local increase of pressure $>>$

collagen fiber angle governed by pressure/stretch ratio

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

fiber reorientation in response to changes in loading

kuhl & holzapfel [2007]

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

example - mitral valve leaflet
are collagen fibers aligned w/maximum principal strains?

Shultz, Rausch, Kuhl [2010]

collagen fiber orientation in the mitral valve leaflet

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 side of the leaflet (right).

Are collagen fibers aligned w/maximum principal strains?

Driessen [2006]

Example - mitral valve leaflet

Example - mitral valve leaflet

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

Remodeling