

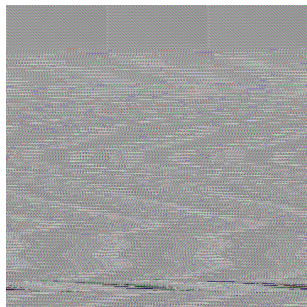
A Continuum Treatment Of Coupled Mass Transport And Mechanics In Growing Soft Biological Tissue

Nutrient transport is pivotal

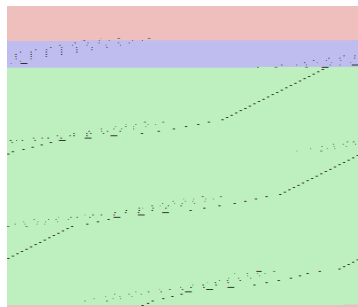
H. Narayanan, K. Garikipati, E. M. Arruda, K. Grosh & S. Calve
University of Michigan
Summer Bioengineering Conference, Vail, CO
June 23rd, 2005

Motivation and definition

Growth/Resorption ~~is~~ *An addition or loss of mass*



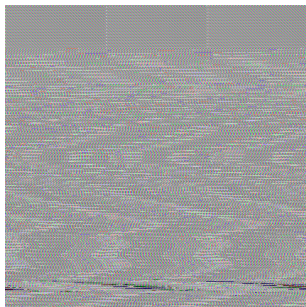
Engineered tendon constructs [Calve et al]



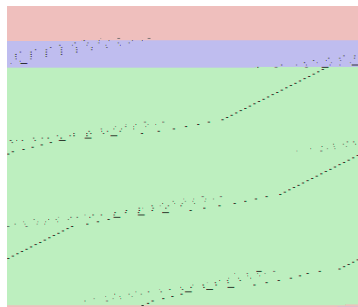
Increasing collagen concentration with age

Motivation and definition

Growth/Resorption ~~is~~ *An addition or loss of mass*



Engineered tendon constructs [Calve et al]



Increasing collagen concentration with age

Open system with multiple species inter-converting and interacting

Modelling challenges and approach

Classical balance laws enhanced via ρ_{ex} and sources

ρ_{solid} Solid ρ_{solid} Collagen, proteoglycans, cells

ρ_{ex} Extra cellular ρ_{ex} fluid

ρ_{solid} Undergoes transport relative to the solid phase

ρ_{ex} Dissolved solutes (sugars, proteins, ...)

ρ_{ex} Undergo transport relative to ρ_{solid}

Modelling challenges and approach

Classical balance laws enhanced via ~~fluxes~~ and sources

~~Ex~~ Solid ~~Ex~~ Collagen, proteoglycans, cells

~~Ex~~ Extra cellular ~~Ex~~

~~Ex~~ Undergoes transport relative to the solid phase

~~Ex~~ Dissolved solutes (sugars, proteins, ...)

~~Ex~~ Undergo transport relative to ~~Ex~~

Modelling challenges and approach

Classical balance laws enhanced via fluxes and sources

~~100%~~ Solid ~~100%~~ Collagen, proteoglycans, cells

~~100%~~ Extra cellular ~~100%~~

~~100%~~ Undergoes transport relative to the solid phase

~~100%~~ Dissolved solutes (sugars, proteins, ...)

~~100%~~ Undergo transport relative to ~~100%~~

Brief subset of related literature:

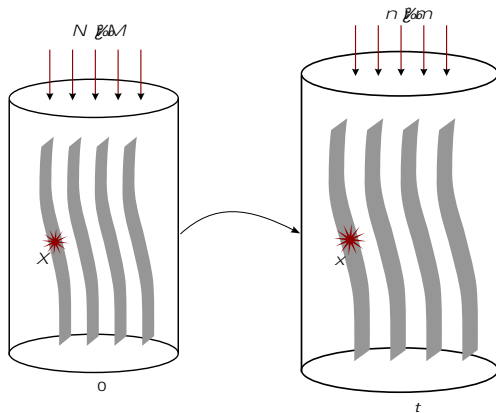
Cowin and Hegedus [1976]

Kuhl and Steinmann [2002]

Sengers, Oomens and Baaijens [2004]

Garikipati et al. *Journal of the Mechanics and Physics of Solids* (52) 1595-1625 [2004]

Mass balance



Species concentration
Species production
Species loss

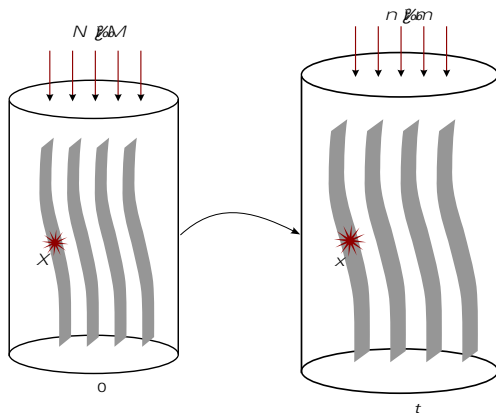
For a species: $\frac{dM}{dt} = \sum \dot{m}_{in} - \sum \dot{m}_{out} + \dot{m}_{gen} - \dot{m}_{cons}$

Solid No boundary conditions

Fluid No source; concentration or boundary conditions

Solute Flux and source; concentration boundary condition

Mass balance



Species concentration
Species production
Species mass

For a species: $\frac{dM}{dt} = \sum \dot{m}_i + \dot{S}$

Solid No flux; no boundary conditions

Fluid No source; concentration or flux boundary conditions

Solute Flux and source; concentration boundary condition

Possibilities for the sources

Simple 1st order rate law

Constituents either solid or fluid

$$f = k^f (f_{ini} - f), \quad c = f$$

Strain Energy Dependencies

Weighted by relative densities

$$f = \frac{c}{c_0} \frac{E}{E_0} f_{ini}$$

Thompson & Johnson (1974)

Enzyme Kinetics

Introducing additional species to the mixture



Thompson (1974)

Possibilities for the sources

Simple 1st order rate law

Constituents either solid or fluid

$$f = k^f (f_{ini}), \quad c = f$$

Strain Energy Dependencies

Weighted by relative densities

$$c = \left(\frac{c}{c_{ini}} \right)^{\gamma} c_{ini}$$

Harrigan & Hamilton [1993]

Enzyme Kinetics introducing additional species to the mixture

Possibilities for the sources

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Constituents either solid or fluid

$$f = k^f (f_{ini} - f), \quad c = f$$

Strain Energy Dependencies

Weighted by relative densities

$$c = \left(\frac{c}{c_{ini}} \right)^{\rho_m} \rho_0$$

Harrigan & Hamilton [1993]

Enzyme Kinetics
Introducing additional species to the mixture

$$s = \frac{\left(\frac{s_{max}}{s_m + s} \right)}{\left(\frac{s_{max}}{s_m + s} \right)} \text{ cell}, \quad c = s$$

Michaelis Menten [1913]

Enzyme Kinetics

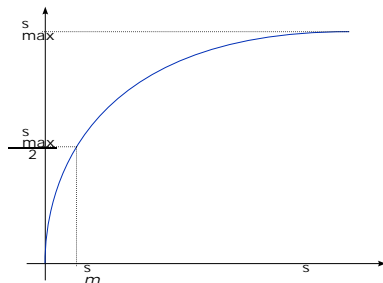


k_1 - Association of substrate and enzyme

k_{-1} - Dissociation of unaltered substrate

k_2 - Formation of product

$$s_m = \frac{(k_2 + k_{-1})}{k_1}$$



$$\overline{t} = \mathcal{E}_{00} \quad \mathcal{E}_{00}^M$$

Constitutive relations for mixtures

Compatible with dissipation inequality

Fluid relative to collagen

$$\mathbf{M}^f = \mathbf{D}^f \mathbf{F}^T \mathbf{g} + \mathbf{F}^T \mathbf{D}^f \mathbf{F} \quad (\mathbf{e}^f \text{ relative to } \mathbf{F})$$

Solute (proteins, sugars, nutrients, ...) relative to fluid

$$\mathbf{V}^s = \mathbf{V}^s \mathbf{V}^f$$

$$\mathbf{M}^s = \mathbf{D}^s \mathbf{V}^f \quad (\mathbf{e}^s \text{ relative to } \mathbf{V}^f)$$

\mathbf{D}^f and \mathbf{D}^s Positive semi-definite mobility tensors

Magnitudes from literature, e.g. Mauck et al. [2003]

Constitutive relations for mixtures

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$$\mathbf{V}^s = \mathbf{V}^s \mathbf{V}^f$$
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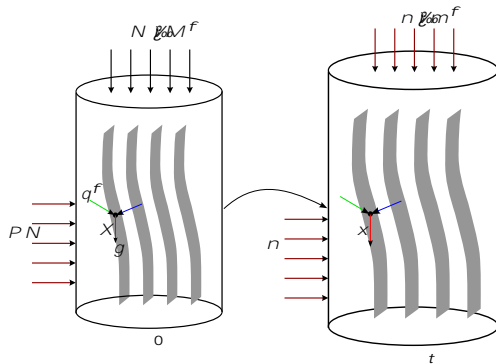
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Momentum balance

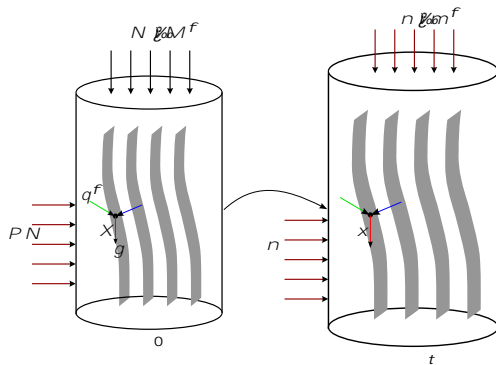


f Fluid concentration
 V Solid velocity
 V^f Fluid relative velocity
 g Body force
 q^f Interaction force
 P^f Partial stress

For the fluid, velocity relative to the solid: $V^f = (1/f)FM^f$

$$f \gamma V + V^f = f g + q^f + P^f / f (V + V^f) M^f$$

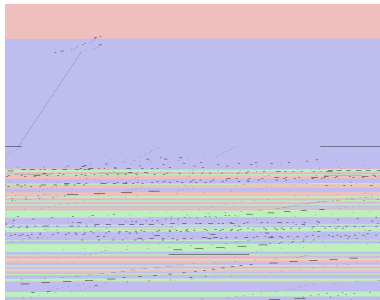
Momentum balance



c^f Fluid concentration
 V Solid velocity
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For the fluid, velocity relative to the solid: $V^f = (1/c^f) \nabla M^f$
 $\frac{d}{dt} V + V^f = g + q^f + \nabla \cdot (V + V^f) M^f$

Constitutive relations for partial stress

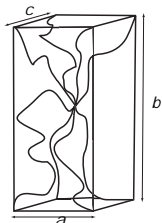


Stress-strain response curves of self organized tendon [Arruda et al]

~~Not~~ Hyper-elastic material compatible with dissipation inequality

Worm-like chain model based internal energy density

$$\rho^e \hat{\rho}^e(\mathbf{F}^e, \rho^e)$$



$$= \frac{Nk}{4A} \frac{r^2}{2L} + \frac{L}{4(1 - \rho_{\text{ord}}/L)} \rho_{\text{ord}} \frac{r}{4}$$

$$\rho_{\text{ord}} \frac{Nk}{4} \frac{\overline{2A}}{2L/A} + \frac{1}{4(1 - \rho_{\text{ord}})} \frac{1}{\overline{2A/L}} \rho_{\text{ord}} \frac{1}{4} \log \left(\frac{a^2}{1} \frac{b^2}{2} \frac{c^2}{3} \right)$$

$$+ \frac{1}{2} \left(\frac{1}{2} \rho_{\text{ord}} \right) \rho_{\text{ord}} + 2 \frac{1}{2} : \mathbf{E}^e$$

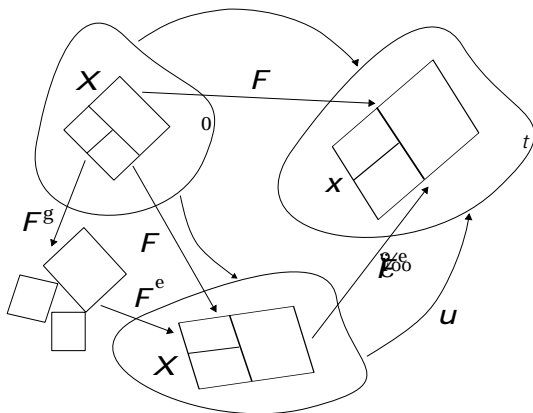
ρ_{ord} Embed in multi chain model [Bischoff et al.]

$$r = \frac{1}{2} \sqrt{a^2 \frac{e^2}{1} + b^2 \frac{e^2}{2} + c^2 \frac{e^2}{3}}$$

ρ_{ord}^e Elastic stretches along a, b, c

$$\rho_i^e = \frac{N_i \rho_{\text{ord}}^e N_i}{N_i \rho_{\text{ord}}^e N_i}$$

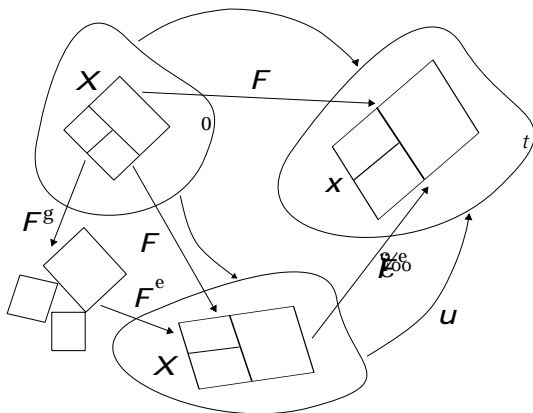
Growth kinematics



$$\mathcal{E}_{00} F = \mathcal{E}_{00} F^e F^g ; F^e = \mathcal{E}_{00}^{-1} F ; \text{Internal stress due to } F^e$$

isotropic swelling due to growth: $F^g = \frac{\rho_{ini}}{\rho_{00}} \mathbf{1}$

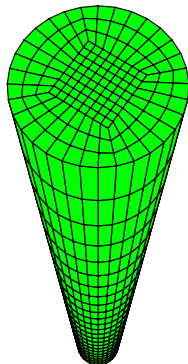
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$$\mathcal{E}_{00} \text{Isotropic swelling due to growth: } F^g = \frac{1}{\phi_{ini}}$$

Example of coupled computation



Simulating a tendon immersed in a nutrient rich bath

Biphasic model

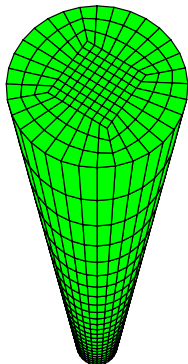
Two water like fluid phases for collagen and proteoglycan
Solid matrix is compressible
 $\sigma = \frac{1}{2} \lambda (\text{tr}(\epsilon))^2 + \mu \text{tr}(\epsilon)$

Fluid mobility $D_{ij}^f = 10^{-8} \delta_{ij}$,
Han et al. [2000]

First order rate law:

$$\dot{c} = k(c - c_{ini}), \quad c = c_{ini}$$

Example of coupled computation



• Simulating a tendon immersed in a nutrient rich bath

• Biphasic model

- worm-like chain model for collagen
- ideal nearly incompressible fluid

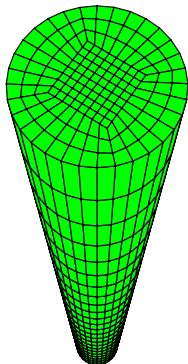
$$\hat{e}^f = \frac{1}{2} (\det(\mathbf{F}^e)^2 - 1)^2$$

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Han et al. [2000]

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$$\dot{\mathbf{f}} = k^f (\mathbf{f} - \mathbf{f}_{in}), \quad \dot{\mathbf{c}} = k^c$$

Example of coupled computation



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$$\hat{e}^f = \frac{1}{2} (\det(\mathbf{F}^{e^f}) - 1)^2$$

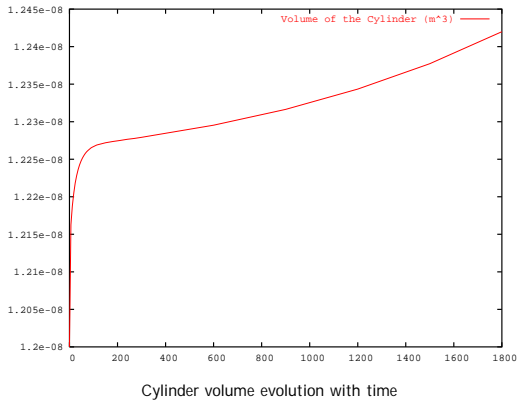
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$$\dot{c}^f = k^f (c^f - c_{ini}^f), \quad c = c^f$$

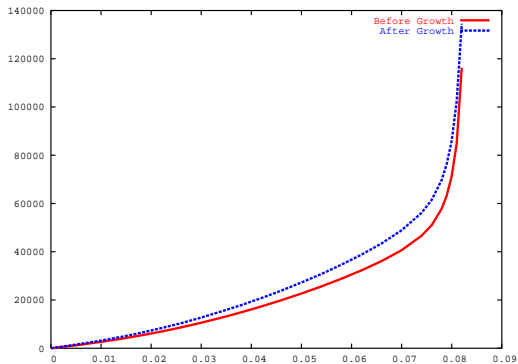
Results and inferences

Collagen concentration evolution



Results and inferences

Collagen concentration evolution



Stress vs Extension curves

Summary and further work

✓ Physiologically relevant continuum formulation describing growth in an open system ✓ Consistent with mixture theory

✓ Relevant driving forces arise from thermodynamics
✓ Coupling with mechanics

✓ Gained insights into the problem

- Issues of saturation and growth
- Saturation and Fickian diffusion
- Configurations and physical boundary conditions

✓ More careful treatment of biochemistry ✓ Nature of sources

✓ Formulated a theoretical framework for remodelling

✓ Engineering and characterization of growing, functional biological tissue to drive and validate modelling

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