

# Computational Modelling of Mechanics and Transport in Growing Tissue

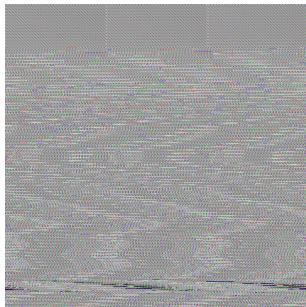
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University of Michigan

Eighth U.S. National Congress on Computational Mechanics

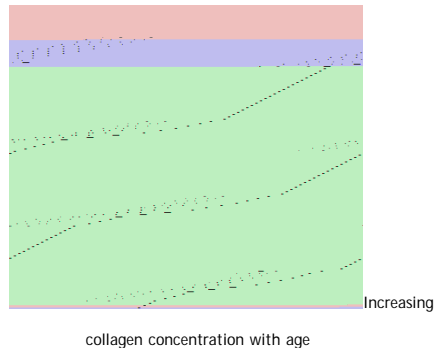
July 25<sup>th</sup>, 2005 Austin, TX

# Motivation and definition

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

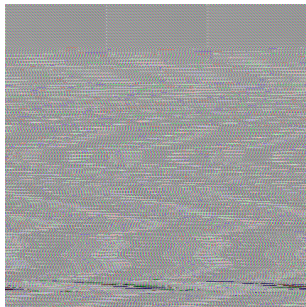


Engineered tendon constructs [Calve et al, 2004]

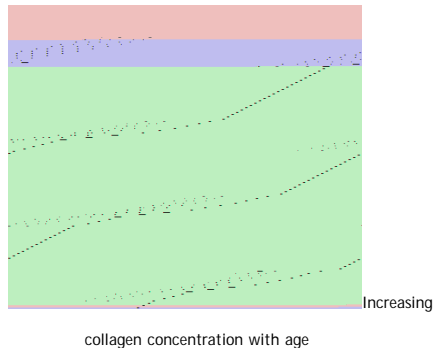


# Motivation and definition

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



Engineered tendon constructs [Calve et al, 2004]



Open system with multiple species inter-converting and interacting

# Modelling approach

Classical balance laws enhanced via  $\rho_{\text{ec}}$  and sources

$\rho_{\text{ec}}$  Solid  $\rho_{\text{ec}}$  Collagen, proteoglycans, cells

$\rho_{\text{ec}}$  Extra cellular  $\rho_{\text{ec}}$

$\rho_{\text{ec}}$  Undergoes transport relative to the solid phase

$\rho_{\text{ec}}$  Dissolved solutes (sugars, proteins, ...)

$\rho_{\text{ec}}$  Undergo transport relative to  $\rho_{\text{ec}}$

# Modelling approach

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

~~Loss~~ Solid ~~Loss~~ Collagen, proteoglycans, cells

~~Loss~~ Extra cellular ~~Loss~~

~~Loss~~ Undergoes transport re lative to the solid phase

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

~~Loss~~ Undergo transport relative to ~~loss~~

# Modelling approach

Classical balance laws enhanced via fluxes and sources

$\rho_0$  Solid  $\rho_0$  Collagen, proteoglycans, cells

$\rho_0$  Extra cellular  $\rho_0$

$\rho_0$  Undergoes transport relative to the solid phase

$\rho_0$  Dissolved solutes (sugars, proteins, ...)

$\rho_0$  Undergo transport relative to  $\rho_0$

Brief subset of related literature:

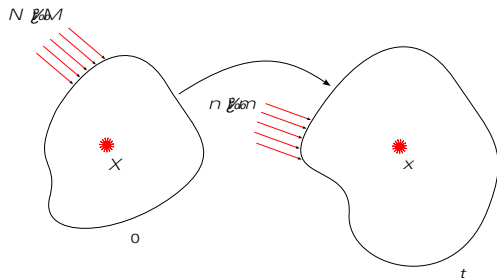
Cowin and Hegedus [1976]

Kuhl and Steinmann [2002]

Sengers, Oomens and Baaijens [2004]

Garikipati et al. *Journal of the mechanics and physics of solids* (52) 1595-1625 [2004]

# Balance of mass



$\frac{\partial \rho}{\partial t}$  Species concentration  
 $\frac{\partial \rho}{\partial t}$  Species production  
 $M$  Species mass

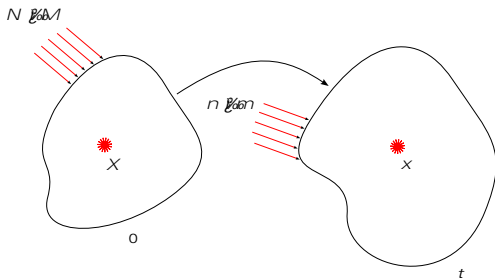
For a species:  $\frac{\partial \rho}{\partial t} = \frac{\partial \rho}{\partial t} \times M$

Solid No No boundary conditions

Fluid No source; Concentration or boundary conditions

Solute Flux and source; Concentration boundary condition

# Balance of mass



$\rho$  Species concentration  
 $\sigma$  Species production  
 $M$  Species mass

For a species: 
$$\frac{dM}{dt} = \int_V \sigma \, dV + \int_{\partial V} \rho \mathbf{n} \cdot \mathbf{v} \, dA$$

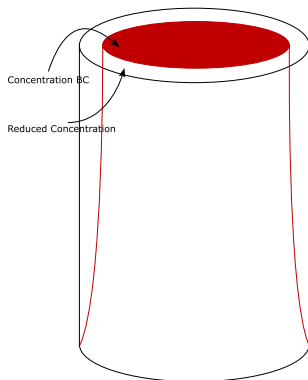
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# Configuration and physical boundary conditions



Boundary condition specification

$$\frac{d}{dt} \left( \int_{\Omega} c^i \, dV \right) + \int_{\partial\Omega} c^i \mathbf{v} \cdot \mathbf{n} \, dA = \int_{\Omega} \sigma^i \, dV + \int_{\partial\Omega} \gamma^i \, dA$$

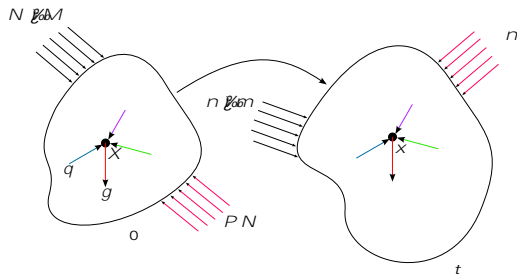
$c^i$  Current species concentration

$\sigma^i$  Current species production

$\mathbf{v}$  Current species velocity

$\mathbf{v}$  Solid velocity

# Balance of momentum



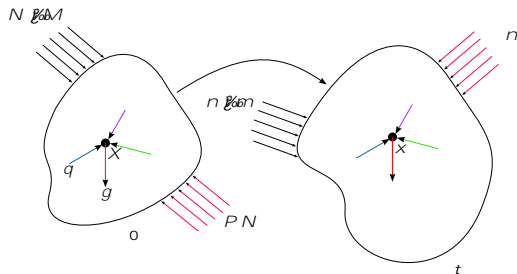
- $\rho$  Species concentration
- $V$  Solid velocity
- $V$  Species relative velocity
- $g$  Body force
- $q$  Interaction force
- $P$  Partial stress

For a species, velocity relative to the solid:  $V = (1/\rho) \nabla \cdot \mathbf{F}$

$$\rho \frac{d}{dt} (V + V) = \rho (g + q) + \nabla \cdot (\rho (V + V))$$

Negligible contribution to mechanics from dissolved solutes

# Balance of momentum



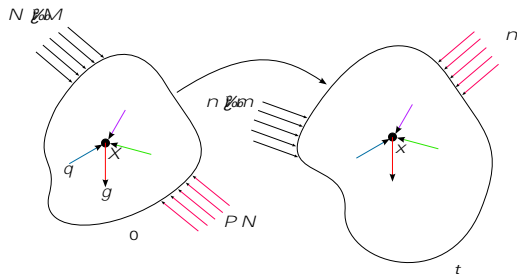
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For a species, velocity relative to the solid:  $\mathbf{V} = (1/\rho) \nabla F M$

$$\rho \frac{d}{dt} (\mathbf{V} + \mathbf{V}) = \rho (\mathbf{g} + \mathbf{q}) + \nabla \cdot (\rho (\mathbf{V} + \mathbf{V})) M$$

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# Balance of momentum



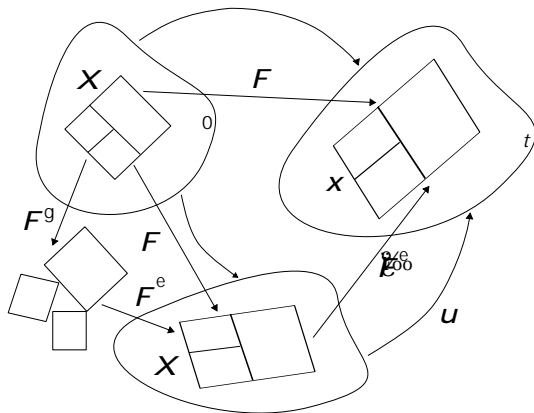
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# Growth kinematics

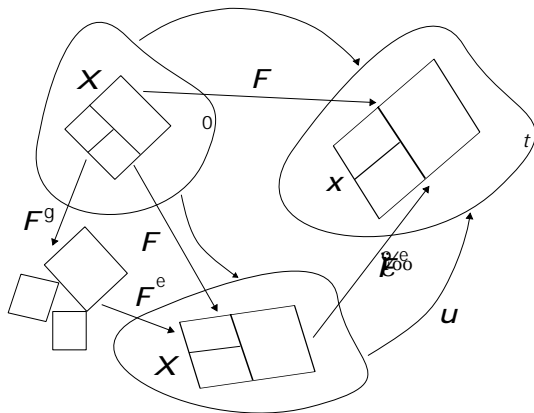


$$\mathbb{E}_{\infty} F = \mathbb{E}_{\infty}^e F^e F^g ; F^e = \mathbb{E}_{\infty}^e F^e ; \text{Internal stress due to } F^e$$

%isotropic swelling due to growth:  $F^g = \frac{\phi}{\phi_{\text{int}}} 1$

%Saturation and swelling

# Growth kinematics

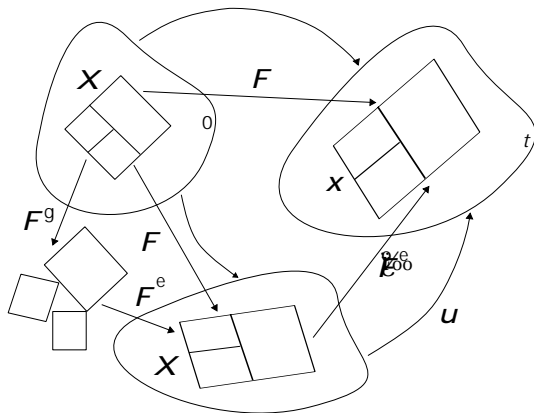


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# Growth kinematics

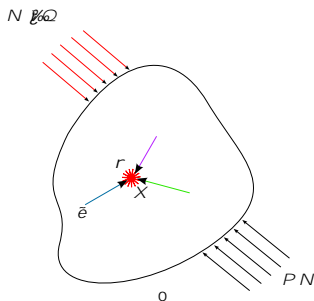


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Saturation and swelling

# Energy balance and entropy inequality

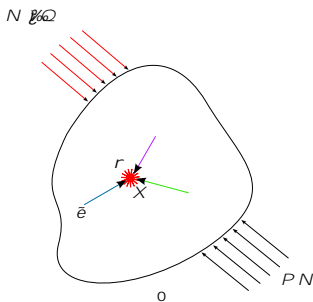


- $\rho$  Species concentration
- $e$  Specific internal energy
- $P$  Partial stress
- $F$  Deformation gradient
- $V$  Species relative velocity
- $Q$  Partial heat flux
- $r$  Species heat supply
- $\tilde{e}$  Energy transfer
- $M$  Species mass

$$\rho \frac{de}{dt} = P : \dot{F} + P : \sum_x V \otimes \otimes Q + r + \rho \tilde{e} \otimes \otimes e \otimes (M)$$



# Energy balance and entropy inequality



- $\rho_0$  Species concentration
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- $F$  Deformation gradient
- $V$  Species relative velocity
- $Q$  Partial heat
- $r$  Species heat supply
- $\tilde{e}$  Energy transfer
- $M$  Species mass
- $S$  Species entropy
- $T$  Temperature

$$\rho_0 \frac{de}{dt} = P : \dot{F} + P : \nabla X V + \nabla X Q + r + \rho_0 \tilde{e} + \nabla X M$$

$$= \rho_0 \frac{de}{dt} = \frac{r}{\rho_0} + \frac{\nabla X M}{\rho_0} + \frac{\nabla X Q}{2}$$

# Constitutive relations for tissues

Combine 1st and second laws to get dissipation inequality

Constitutive hypothesis  $e = \hat{e}(\mathbf{F}^e, \theta, \dots)$

Consistent constitutive relations

Fluid relative to collagen

$$\mathbf{M}^f = \mathbf{D}^f \left( \frac{1}{\rho_0} \mathbf{F}^T \mathbf{g} + \mathbf{F}^T \chi(\mathbf{D}^f) \chi(e^f) \right)$$

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

$$\mathbf{V}^s = \mathbf{V}^s \chi(\mathbf{D}^s)$$

$$\mathbf{M}^s = \mathbf{D}^s \chi(e^s)$$

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

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

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

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

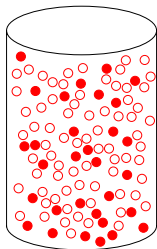
$$\mathbf{V}^s = \mathbf{V}^s \times \mathbf{V}^f$$

$$\mathbf{M}^s = \mathbf{D}^s (\times (\mathbf{e}^s \times \mathbf{s}))$$

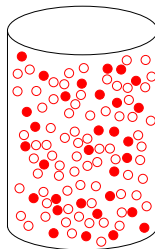
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# Saturation and Fickian diffusion



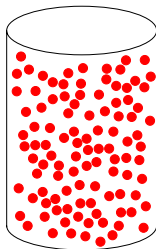
Configuration 1



Configuration 2

Change in configurational entropy with distribution of solute particles ... if solvent is not saturated with solute

# Saturation and Fickian diffusion



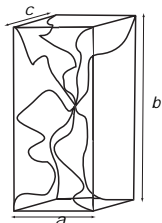
Only possible configuration

~~100%~~ Saturated      Single configuration      ~~100%~~ No Fickian diffusion

~~100%~~ Still have concentration-gradient driven transport due to stress gradient contribution to ~~100%~~

# Worm-like chain model based internal energy density

$$\rho^c \bar{\epsilon}^c(\mathbf{F}^{e^c}, \mathbf{c}_0)$$



$$= \frac{Nk}{4A} \frac{r^2}{2L} + \frac{L}{4(1 - \ell_{\infty} r/L)} \ell_{\infty} \frac{r}{4}$$

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

$$+ \frac{1}{2} (J^e \ell_{\infty}^2 \ell_{\infty}^2) + 2 \frac{1}{2} : \mathbf{E}^{e^c}$$

Embed in multi chain model [Bischoff et al., 2002]

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

$\ell_{\infty}^e$  Elastic stretches along a, b, c

$$\ell_i^e = \frac{N_i \ell_{\infty}^e N_i}{N_i \ell_{\infty}^e N_i}$$

# Computational formulation details

- Implementation in FEAP

- Coupled implementation; Staggered scheme  
(Armero [1999], Garikipati et al. [2001])

- Nonlinear projection methods to treat incompressibility  
(Simo et al. [1985])

- Energy-momentum conserving algorithm for dynamics  
(Simo & Tarnow [1992a,b])

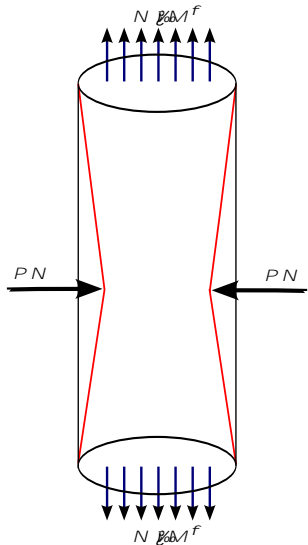
- Backward Euler for time-dependent mass balance

- Mixed method for stress/strain gradient-driven flows  
(Garikipati et al. [2001])

- Large advective terms require stabilization



# Examples of coupled computation & Constriction



• Simulating a tendon immersed in a bath

• Constrict it to force  $\frac{1}{M}$  and dissolved nutrient  $\frac{1}{M}$  guided tendon growth

• Biphasic model

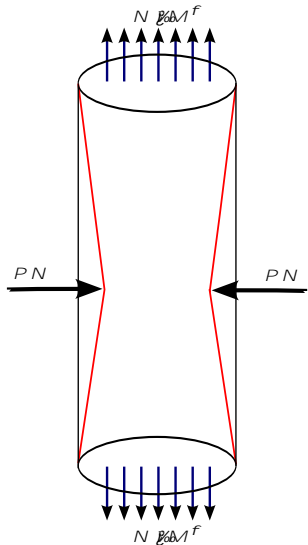
• Fluid mobility  $D_{ij}^f = 1 \times 10^{-8} \text{ } \mu\text{m}^2/\text{s}$   
 Han et al. [2000]

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• First order rate law:

$$r = k^f (c - c_{\text{int}}), \quad c = c_{\text{int}}$$

# Examples of coupled computation & Constriction



• Simulating a tendon immersed in a bath

• Constrict it to force  $\nabla \phi$  and dissolved nutrient  $\nabla \mu$  guided tendon growth

• Biphasic model

- Worm-like chain model for collagen
- Ideal nearly incompressible  $\nabla \phi$

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

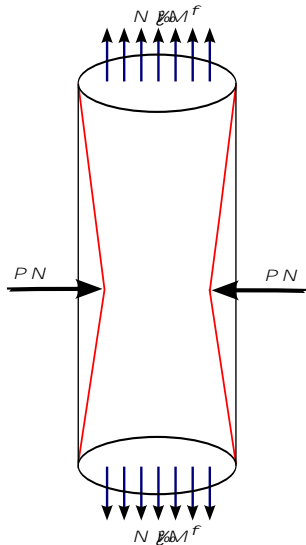
• Fluid mobility  $D_{ij}^f = 10^{-8} \delta_{ij}$ ,

Han et al. [2000]

• First order rate law:

$$\dot{c} = k^+ (c_{\text{lim}} - c), \quad \dot{c} = k^- c$$

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• Simulating a tendon immersed in a bath

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$$f = k^f (f - f_{0ini}), \quad c = f$$

# Results and inferences

- Total  $\dot{\epsilon}_v$  in the vertical direction
- Stress driven diffusion

# Results and inferences

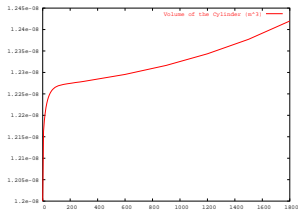
~~100~~ Regions of high ~~100~~ concentration  
Faster growth

~~100~~ Relaxation after constriction concludes

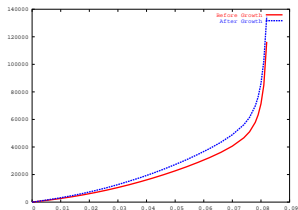
# Swelling of a tendon immersed in a bath

Collagen concentration evolution

Volume evolution curve



Stress-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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