Coupled Mechanics and Transport in Growing Soft Tissue

Nutrient transport is pivotal

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University of Michigan

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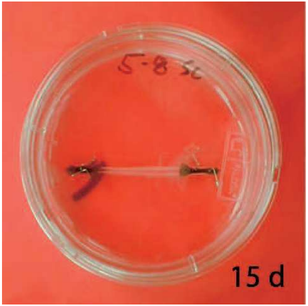
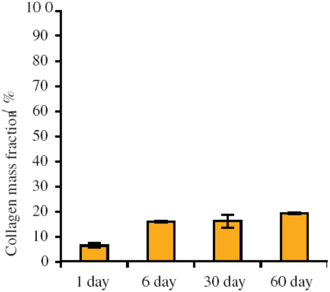
June 3rd, 2005

Motivation and definition

Growth – An addition or loss of mass



Engineered tendon constructs [Calve et al]



Increasing collagen concentration with age

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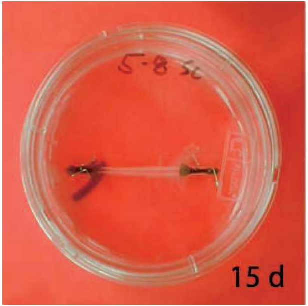

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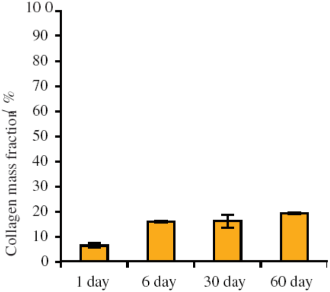

Increasing collagen concentration with age

Open system with multiple species inter-converting and interacting

Modelling approach

Classical balance laws enhanced via fluxes and sources

- Solid – Collagen, proteoglycans, cells
- Extra cellular fluid
  – diffuses relative to the solid phase
- Dissolved solutes (sugars, proteins, . . .)
  – undergo transport relative to fluid

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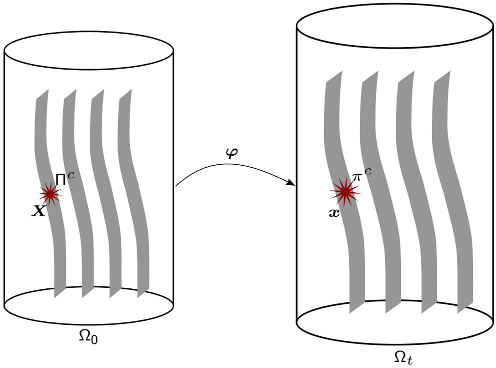
Brief subset of related literature:

- 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]*

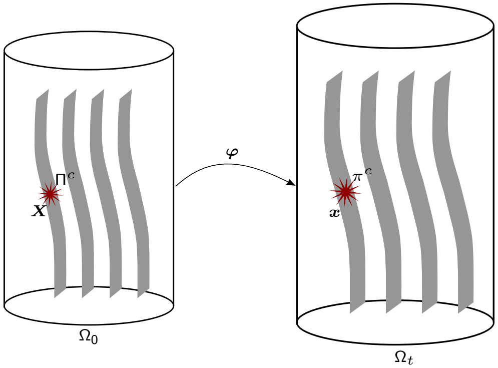
The balance of mass



ρ^c – Collagen concentration
Π^c – Collagen production

- For collagen: $$\frac{\partial \rho^c}{\partial t} = \Pi^c$$
- No flux; No boundary conditions

The balance of mass



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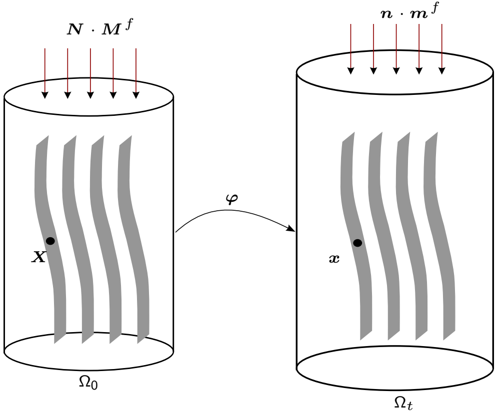
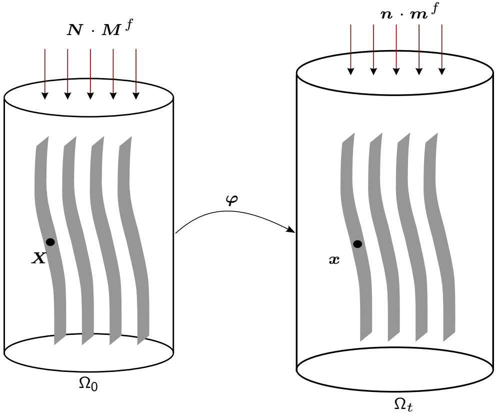


ρ^f – Fluid concentration
M^f – Fluid flux

- For the fluid: $$\frac{\partial \rho^f}{\partial t} = -\nabla \cdot M^f$$
- No source; Concentration or flux boundary conditions – *Tissue exposed to fluid in a bath, fluid injected in at the boundary*

The balance of mass



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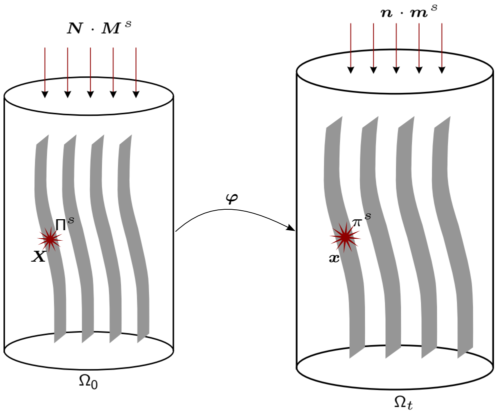

ρ^s – Solute concentration
Π^s – Solute production
$\boldsymbol{M}^s$ – Solute flux

- For a solute: $$\frac{\partial \rho^s}{\partial t} = \Pi^s - \boldsymbol{\nabla} \cdot \boldsymbol{M}^s$$
- Flux and source; Concentration boundary condition – *Tissue exposed to solute in solution in a bath*

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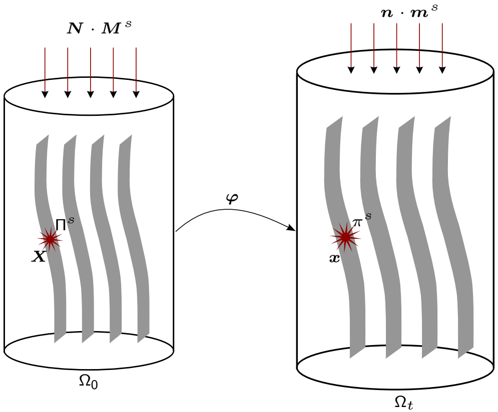

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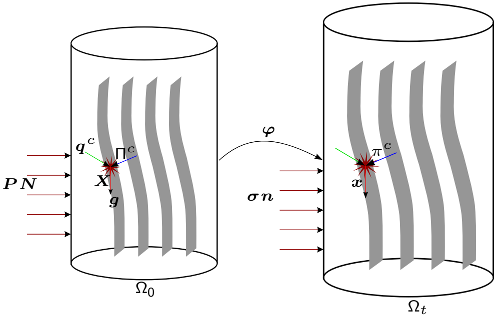
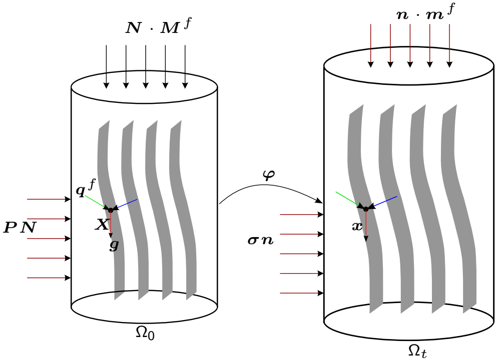
The balance of momentum



ρ^c – Collagen concentration
$\boldsymbol{V}$ – Solid velocity
$\boldsymbol{g}$ – Body force
$\boldsymbol{q}^c$ – Interaction force
$\boldsymbol{P}^c$ – Partial stress

- For collagen: $$\rho^c \frac{\partial \boldsymbol{V}}{\partial t} = \rho^c \left(\boldsymbol{g} + \boldsymbol{q}^c \right) + \boldsymbol{\nabla} \cdot \boldsymbol{P}^c$$

The balance of momentum

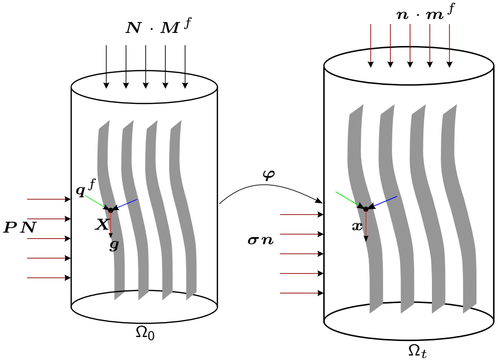


ρ^f – Fluid concentration
V – Solid velocity
V^f – Fluid relative velocity
g – Body force
q^f – Interaction force
P^f – Partial stress

- For the fluid, velocity relative to the solid: $V^f = (1/\rho^f) F M^f$

$$\rho^f \frac{\partial}{\partial t}\left(V + V^f\right) = \rho^f\left(g + q^f\right) + \nabla \cdot P^f - (\nabla(V + V^f))M^f$$

The balance of momentum



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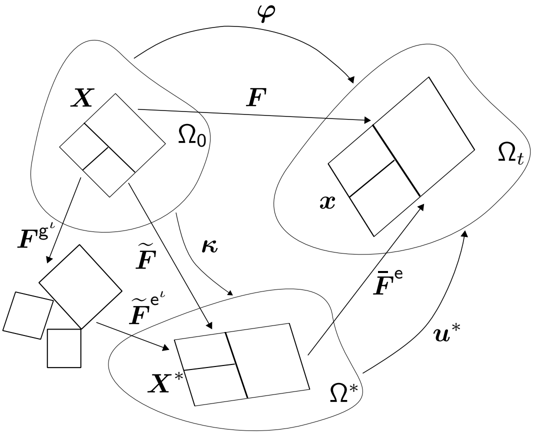
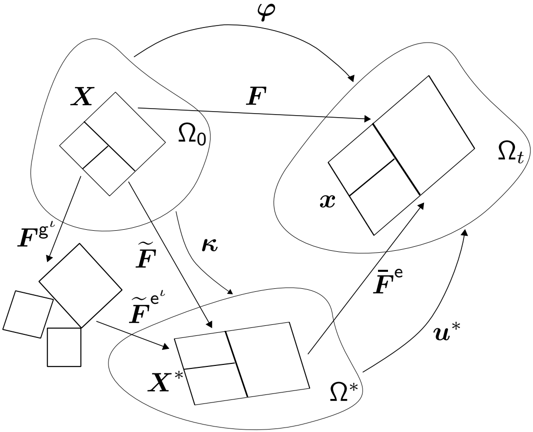
Growth kinematics



- $\boldsymbol{F} = \bar{\boldsymbol{F}}^{e} \widetilde{\boldsymbol{F}}^{e^\iota} \boldsymbol{F}^{g^\iota}$
- Internal stress due to $\widetilde{\boldsymbol{F}}^{e^\iota}$

Growth kinematics



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- Internal stress due to $\widetilde{\boldsymbol{F}}^{\mathrm{e}^\iota}$

Constitutive relations for fluxes

- Combine first and second laws to get dissipation inequality
- Constitutive hypothesis $e^\iota = \hat{e}^\iota(\boldsymbol{F}^{\mathsf{e}^\iota}, \rho^\iota, \eta^\iota)$
  $\Rightarrow$ consistent constitutive relations
- Fluid flux relative to collagen
  $\boldsymbol{M}^f = \boldsymbol{D}^f\left(\rho^f \boldsymbol{F}^T \boldsymbol{g} + \boldsymbol{F}^T \boldsymbol{\nabla}\cdot \boldsymbol{P}^f - \boldsymbol{\nabla}(e^f - \theta\eta^f)\right)$
- Solute flux (proteins, sugars, nutrients, ...) relative to fluid
  $\widetilde{\boldsymbol{V}}^s = \boldsymbol{V}^s - \boldsymbol{V}^f$
  $\widetilde{\boldsymbol{M}}^s = \boldsymbol{D}^s\left(-\boldsymbol{\nabla}(e^s - \theta\eta^s)\right)$
- $\boldsymbol{D}^f$ and $\boldsymbol{D}^s$ – Positive semi-definite mobility tensors
  Magnitudes from literature, e.g. Mauck et al. [2003]

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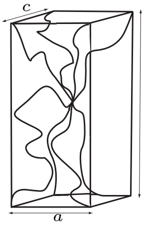
Worm-like chain model for collagen

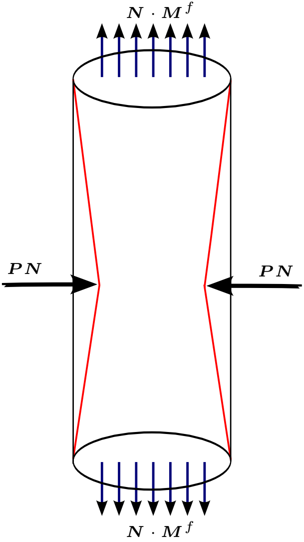
$$\widetilde{\rho}^{\mathsf{c}}\hat{e}^{\mathsf{c}}(\boldsymbol{F}^{\mathsf{e}^{\mathsf{c}}},\rho^{\mathsf{c}})$$



$$
\begin{aligned}
&= \frac{Nk\theta}{4A}\left(\frac{r^2}{2L}+\frac{L}{4(1-r/L)}-\frac{r}{4}\right)\\
&- \frac{Nk\theta}{4\sqrt{2L/A}}\left(\sqrt{\frac{2A}{L}}+\frac{1}{4(1-\sqrt{2A/L})}-\frac{1}{4}\right)\log(\lambda_1^{a^2}\lambda_2^{b^2}\lambda_3^{c^2})\\
&+ \frac{\gamma}{\beta}(J^{\mathsf{e}^{\iota}\,-2\beta}-1)+2\gamma\mathbf{1}:\boldsymbol{E}^{\mathsf{e}^{\mathsf{c}}}
\end{aligned}
$$

- Embed in multi chain model [Bischoff et al.]
  $r=\frac{1}{2}\sqrt{a^2\lambda_1^{\mathsf{e}^2}+b^2\lambda_2^{\mathsf{e}^2}+c^2\lambda_3^{\mathsf{e}^2}}$
- λ_I^{e} – elastic stretches along a, b, c
  $\lambda_I^{\mathsf{e}}=\sqrt{\boldsymbol{N}_I\cdot\boldsymbol{C}^{\mathsf{e}}\boldsymbol{N}_I}$

Example of coupled computation



- Simulating a tendon immersed in a bath
- Constrict it to force fluid and dissolved nutrient flow $\Rightarrow$ Guided tendon growth
- Biphasic model
  - worm-like chain model for collagen
  - ideal nearly incompressible fluid
    $\rho^f e^f = \frac{1}{2}\kappa(\det(F^{e^f}) - 1)^2$
- Fluid mobility $D^f_{ij} = 1 \times 10^{-8}\delta_{ij}$, Han et al. [2000]
- First order rate law:
  $\Pi^f = -k^f(\rho^f - \rho^f_{0_{ini}}), \quad \Pi^c = -\Pi^f$

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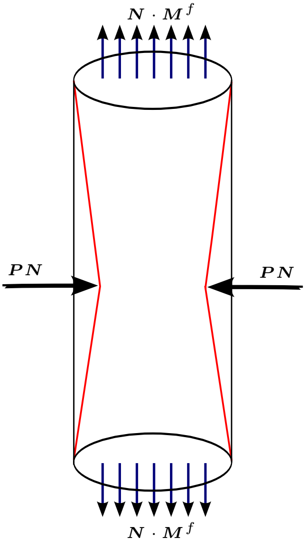

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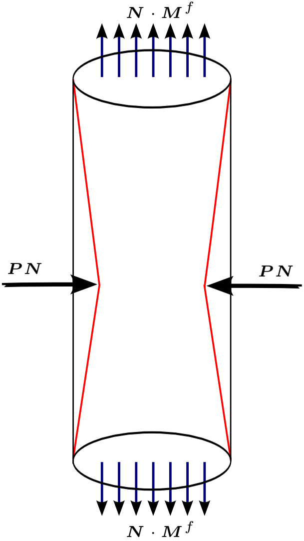

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Results and inferences

- Total flux in the vertical direction
- Stress driven diffusion

Results and inferences

- Regions of high fluid concentration $\Rightarrow$ faster growth
- Relaxation after constriction concludes

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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