A Continuum Treatment of Coupled Mass Transport and Mechanics in Growing Soft Biological Tissue

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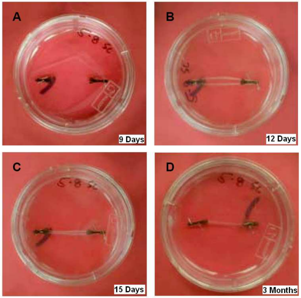
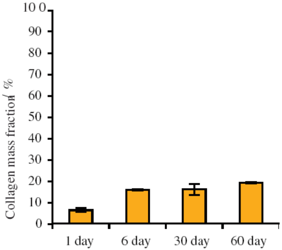
Controlled experiments motivate and validate the descriptive model





- *Growth* – an addition/loss of mass

  … *Increasing collagen concentration with age*

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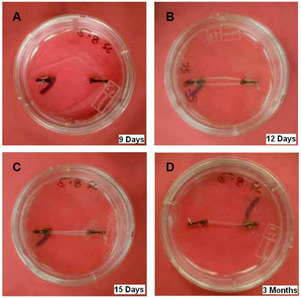

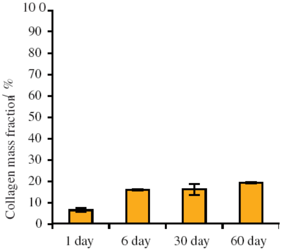

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Multiple species interconverting and interacting

- Collagen, proteoglycans, ECF, solutes (sugars, proteins, . . .)
- Change in concentration – *Growth*
- Interactions via momentum and energy transfer

- Introducing fluxes and sources
- Fluid undergoing transport wrt solid (collagen, cells, proteoglycans)
- Solutes diffusing relative to fluid

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Arising Issues and Our Current Treatment

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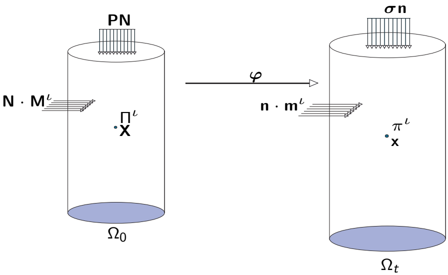
Literature:

- Cowin and Hegedus [1976]
- Kuhl and Steinmann [2002]
- Baaijens et al. [2004]
- *Garikipati et al. – Journal of the Mechanics and Physics of Solids (52) 1595-1625 [2004]*

The Balance of Mass



- For collagen: $$\frac{\partial \rho_0^c}{\partial t} = \Pi^c$$
- No boundary conditions.

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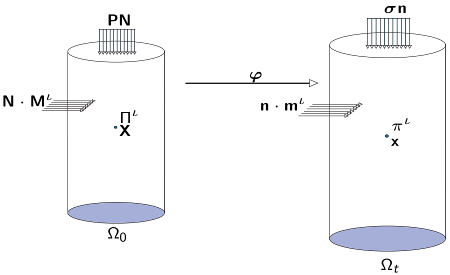

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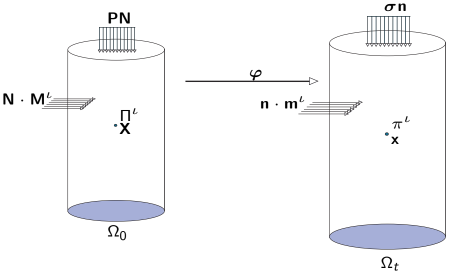

- For the fluid: $$\frac{\partial \rho_0^f}{\partial t} = -\boldsymbol{\nabla}_X \cdot \mathbf{M}^f$$
- Concentration or flux boundary conditions – *Tissue exposed to fluid in a bath, fluid injected in at the boundary*

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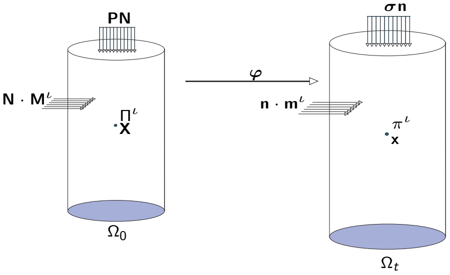

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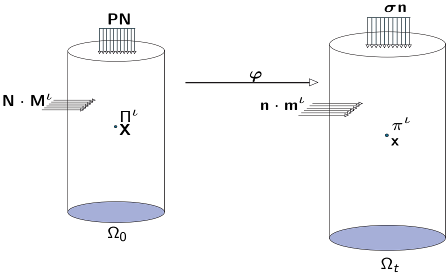

- For a solute: $$\frac{\partial \rho_0^s}{\partial t} = \Pi^s - \boldsymbol{\nabla}_X \cdot \mathbf{M}^s$$
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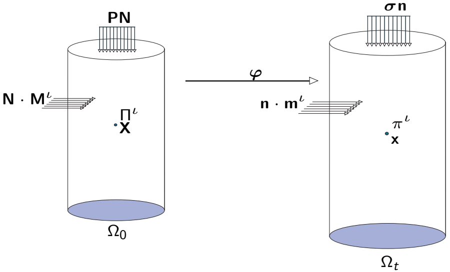

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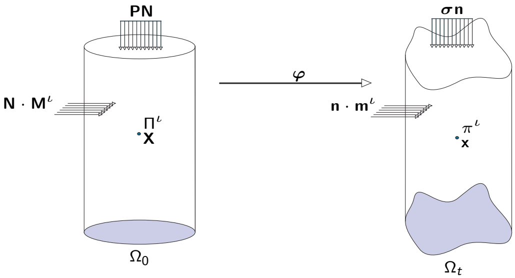

- For collagen: $$\rho_0^c \frac{\partial \mathbf{V}}{\partial t} = \rho_0^c \left(\mathbf{g} + \mathbf{q}^c\right) + \boldsymbol{\nabla}_X \cdot \mathbf{P}^c$$

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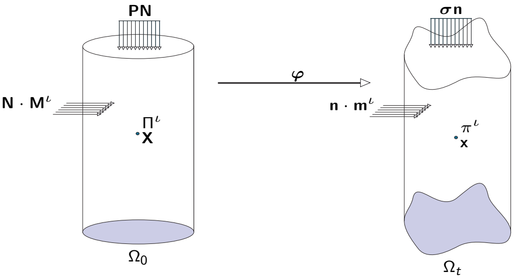

- Velocity relative to the solid $\mathbf{V}^f = (1/\rho_0^f)\mathbf{F}\mathbf{M}^f$
- For the fluid: $\rho_0^f \frac{\partial}{\partial t}\left(\mathbf{V} + \mathbf{V}^f\right) = \rho_0^f\left(\mathbf{g} + \mathbf{q}^f\right) + \nabla_X \cdot \mathbf{P}^f$

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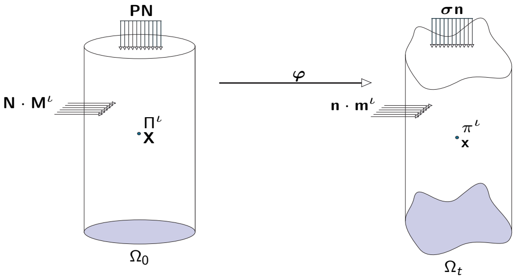

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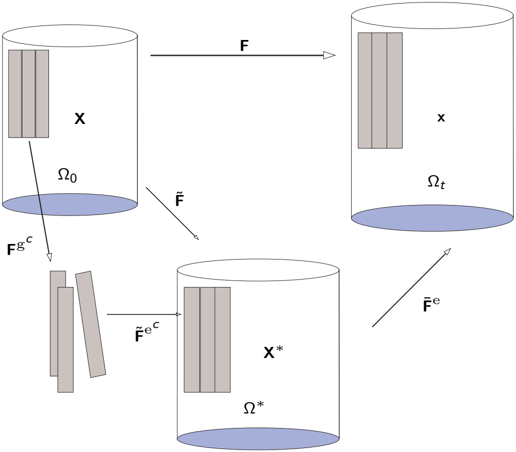
Kinematics of Growth



- $\mathbf{F} = \bar{\mathbf{F}}^{\mathrm{e}} \tilde{\mathbf{F}}^{\mathrm{e}^c} \mathbf{F}^{\mathrm{g}^c}$
- Residual stress due to $\tilde{\mathbf{F}}^{\mathrm{e}^c}$

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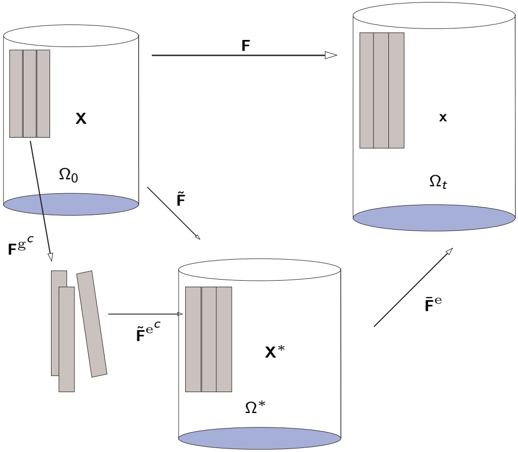

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Constitutive Relations

- Consistent with the dissipation inequality
- Constitutive hypothesis: $e^{\iota} = \hat{e}^{\iota}(\mathbf{F}^{\mathrm{e}^{\iota}}, \rho_0^{\iota}, \eta^{\iota})$
- Collagen Stress: $\mathbf{P}^{c} = \rho_0^{c} \frac{\partial e^{c}}{\partial \mathbf{F}^{\mathrm{e}^{c}}} \mathbf{F}^{\mathrm{g}^{c}-T}$
  - Hyperelastic Material
  - Continuum stored energy function based on the Worm-like chain model
- Fluid Stress: $\mathbf{P}^{f} = \rho_0^{f} \frac{\partial e^{f}}{\partial \mathbf{F}^{\mathrm{e}^{f}}} \mathbf{F}^{\mathrm{g}^{f}-T}$
  - Ideal Fluid
  - $\rho_0^{f} \hat{e}^{f} = \frac{1}{2}\kappa(det(\mathbf{F}^{\mathrm{e}^{f}}) - \mathbf{1})^2$, κ – fluid bulk modulus

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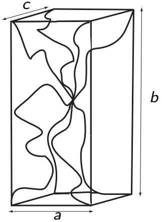
Constitutive Relations – Worm-like Chain Model for Collagen

$$\tilde{\rho}_0^{c}\hat{e}^{c}(\mathbf{F}^{e^c}, \rho_0^c)$$



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

- Embed in Arruda-Boyce Eight Chain Model [1993]
  $$r = \frac{1}{2}\sqrt{a^2\lambda_1^{e^2} + b^2\lambda_2^{e^2} + c^2\lambda_3^{e^2}}$$
- λ_I^{e} – elastic stretches along a, b, c
  $$\lambda_I^{e} = \sqrt{\mathbf{N}_I \cdot \mathbf{C}^{e}\mathbf{N}_I}$$

Constitutive Relations – Fluxes

- Fluid flux relative to collagen
  $$\mathbf{M}^f = \mathbf{D}^f \left(\rho_0^f \mathbf{F}^{\mathrm{T}} \mathbf{g} + \mathbf{F}^{\mathrm{T}} \boldsymbol{\nabla}_X \cdot \mathbf{P}^f - \boldsymbol{\nabla}_X (e^f - \theta \eta^f)\right)$$
- Solute flux (proteins, sugars, nutrients, ...) relative to fluid
  $$\tilde{\mathbf{V}}^s = \mathbf{V}^s - \mathbf{V}^f$$
  $$\tilde{\mathbf{M}}^s = \mathbf{D}^s \left(-\boldsymbol{\nabla}_X (e^s - \theta \eta^s)\right)$$
- $\mathbf{D}^f$ and $\mathbf{D}^s$ – Positive semi-definite mobility tensors

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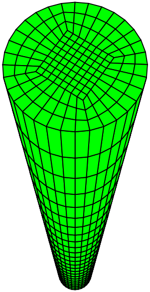
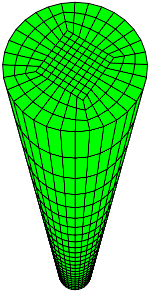


- Biphasic model
  - worm-like chain model for collagen
  - ideal, nearly incompressible interstitial fluid with bulk compressibility of water
  - fluid mobility $D^f_{ij} = 1 \times 10^{-8}\delta_{ij}$, Han et al. [2000]
- "Artificial" sources: $\Pi^{\mathrm{f}} = -k^{\mathrm{f}}(\rho^{\mathrm{f}}_0 - \rho^{\mathrm{f}}_{0_{\mathrm{ini}}})$, $\Pi^{\mathrm{c}} = -\Pi^{\mathrm{f}}$
- Entropy of mixing: $\eta^f_{\mathrm{mix}} = -\frac{k}{\mathcal{M}^f}\log\frac{\rho^f_0}{\rho_0}$



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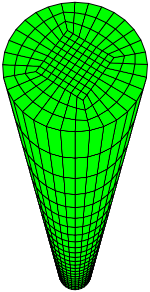

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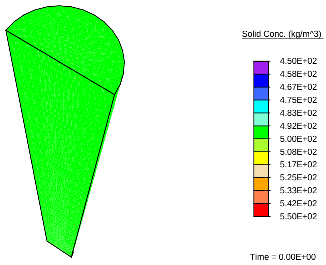
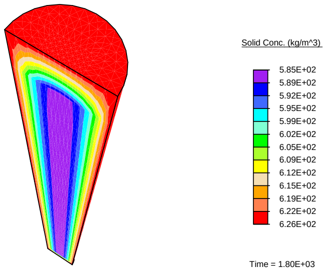
Parameter	Symbol	Value	Units
Chain density	N	7×10^{21}	m^{-3}
Temperature	θ	310.0	K
Persistence length	A	1.3775	–
Fully-stretched length	L	25.277	–
Unit cell axes	$a,\ b,\ c$	9.3, 12.4, 6.2	–
Bulk compressibility factors	$\gamma,\ \beta$	1000, 4.5	–
Fluid bulk modulus	κ	1	GPa
Fluid mobility tensor	$D_{ij} = D\delta_{ij}$	1×10^{-8}	$\mathrm{m}^{-2}\mathrm{sec}$
Fluid conversion reac. rate	k^{f}	$-1. \times 10^{-7}$	sec^{-1}
Gravitational acceleration	$\mathbf{g}$	9.81	$\mathrm{m.sec}^{-2}$
Fluid mol. wt.	$\mathcal{M}^{\mathrm{f}}$	2.9885×10^{-23}	kg

Coupled Computations – Examples – Swelling

Before Growth



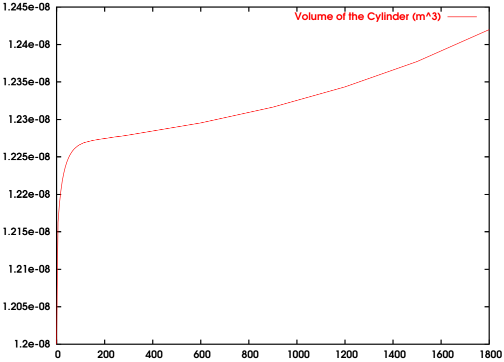
After Growth



- fluid concentration evolution
- fluid sink evolution
- collagen concentration evolution

Coupled Computations – Examples – Swelling

Cylinder Volume Evolution with Time



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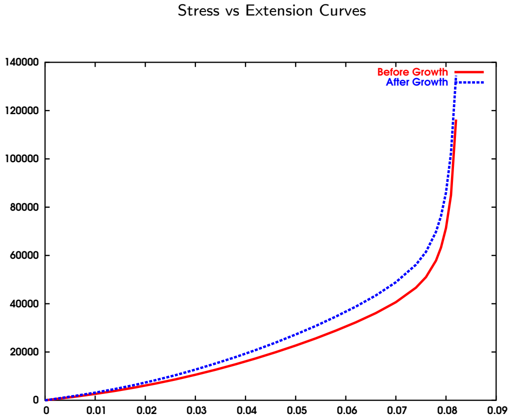

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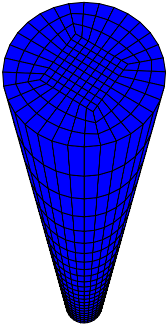
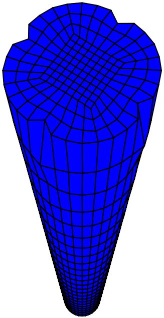
Coupled Computations – Examples – Pinching

Before Pinch



Time = 0.00E+00

After Pinch



Time = 1.00E+01

- fluid concentration evolution
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Summary and Further Work

- Physiologically consistent continuum formulation describing growth in an open system
- Relevant driving forces arise from thermodynamics – coupling with mechanics
- Consistent with mixture theory

- Lattice Boltzmann studies to determine effective transport properties
- Coarse-grained molecular dynamics simulations to investigate the elasticity of collagen fibrils
- Formulated a theoretical framework for the remodelling problem
- Engineering and characterization of growing, functional biological tissue

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