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

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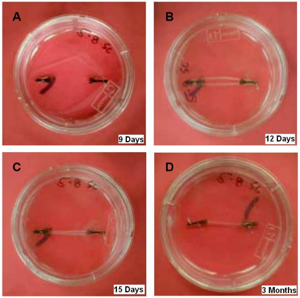
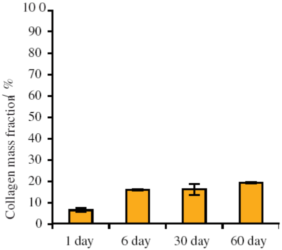
Controlled experiments motivate and validate the descriptive model





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  … *Increasing collagen concentration with age*

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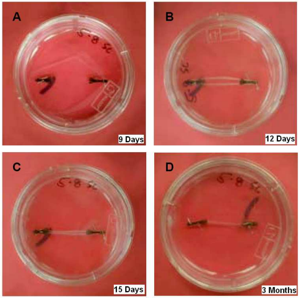

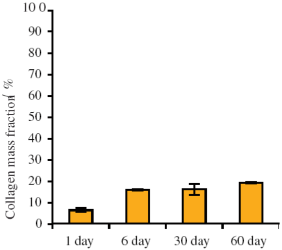

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Multiple species interconverting and interacting

- 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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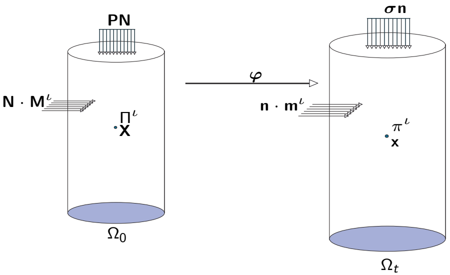
Literature:

- 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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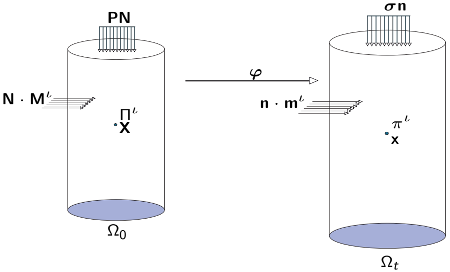

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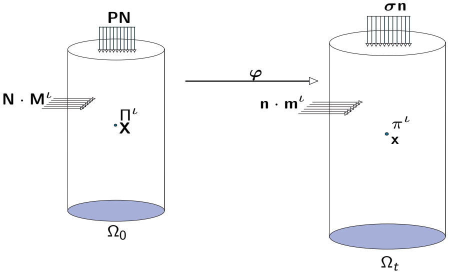

- For the fluid: $$\frac{\partial \rho_0^f}{\partial t} = -\boldsymbol{\nabla}_X \cdot \mathbf{M}^f$$
- Concentration or flux boundary conditions – *Tissue exposed to fluid in a bath, fluid injected in at the boundary*

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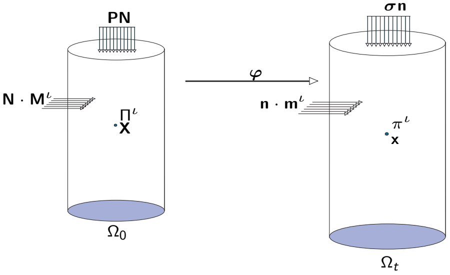

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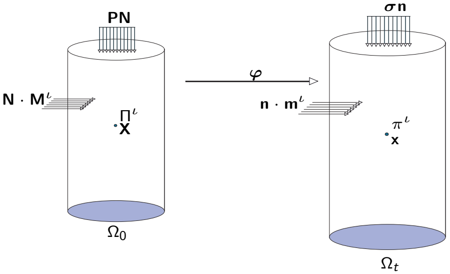

- For a solute: $$\frac{\partial \rho_0^s}{\partial t} = \Pi^s - \boldsymbol{\nabla}_X \cdot \mathbf{M}^s$$
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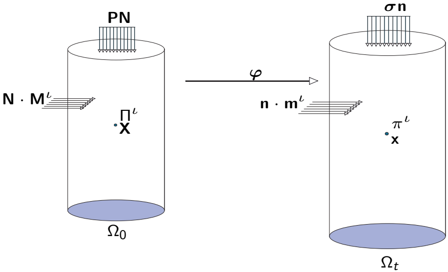

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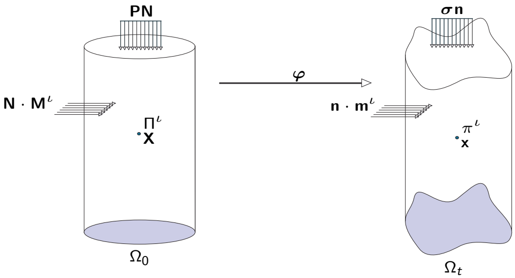
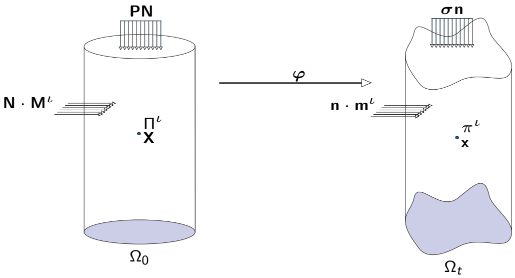
The Balance of Momentum



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



- 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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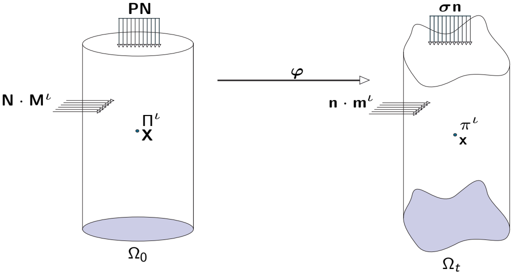

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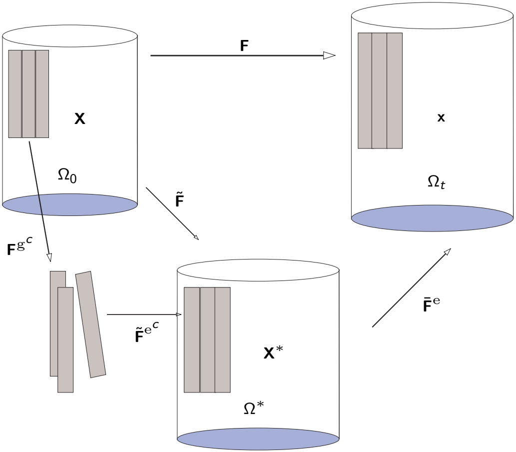
Kinematics of Growth



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

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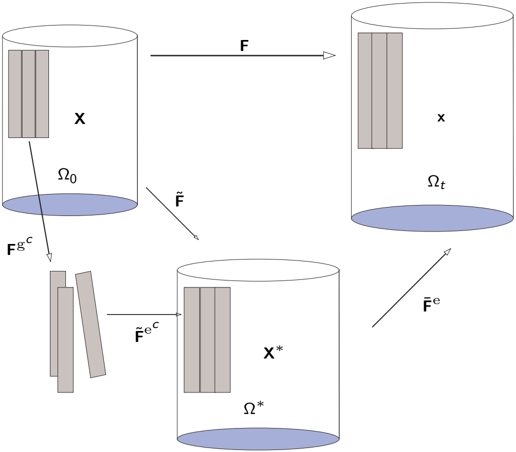

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- Consistent with the dissipation inequality
- Constitutive hypothesis: $e^{\iota} = \hat{e}^{\iota}(\mathbf{F}^{\mathrm{e}^{\iota}}, \rho_0^{\iota}, \eta^{\iota})$
- Collagen Stress: $\mathbf{P}^{c} = \rho_0^{c} \frac{\partial e^{c}}{\partial \mathbf{F}^{\mathrm{e}^{c}}}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

Constitutive Relations

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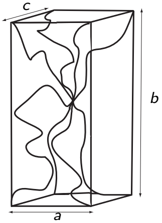
Constitutive Relations – Worm-like Chain Model for Collagen

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



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

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

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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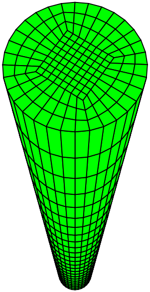
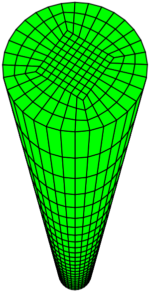


- Biphasic model
  - worm-like chain model for collagen
  - ideal, nearly incompressible interstitial fluid with bulk compressibility of water
  - fluid mobility $D^f_{ij} = 1 \times 10^{-8} \delta_{ij}$, Han et al. [2000]
- "Artificial" sources: $\Pi^{\mathrm{f}} = -k^{\mathrm{f}}(\rho^{\mathrm{f}}_0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



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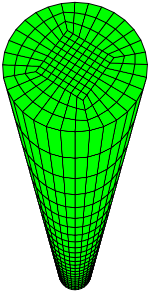

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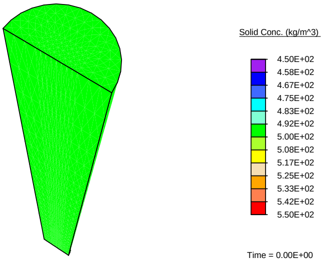
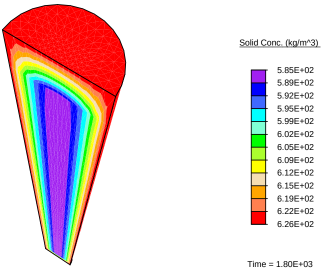
Parameter	Symbol	Value	Units
Chain density	N	7×10^{21}	m^{-3}
Temperature	θ	310.0	K
Persistence length	A	1.3775	–
Fully-stretched length	L	25.277	–
Unit cell axes	$a,\ b,\ c$	9.3, 12.4, 6.2	–
Bulk compressibility factors	$\gamma,\ \beta$	1000, 4.5	–
Fluid bulk modulus	κ	1	GPa
Fluid mobility tensor	$D_{ij} = D\delta_{ij}$	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



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- fluid sink evolution
- collagen concentration evolution

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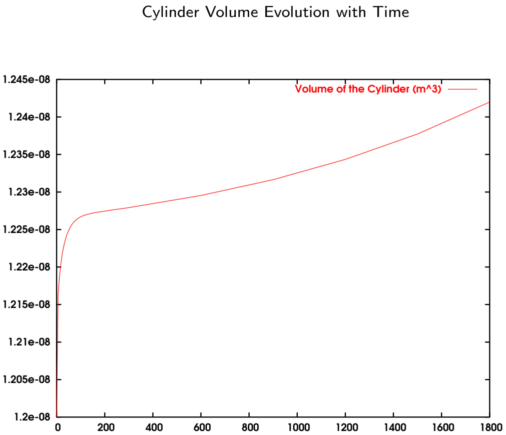

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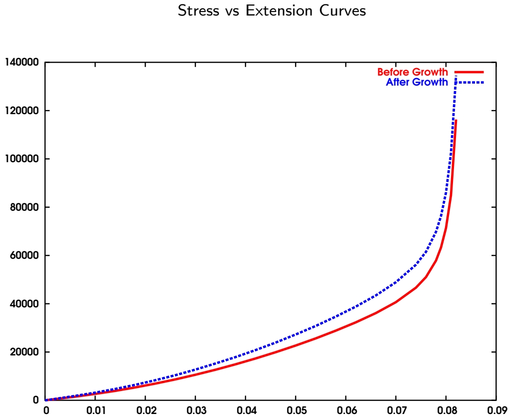

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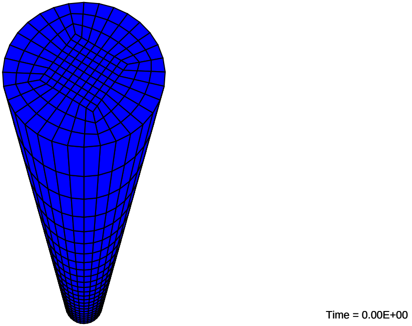
Coupled Computations – Examples – Pinching

Before Pinch



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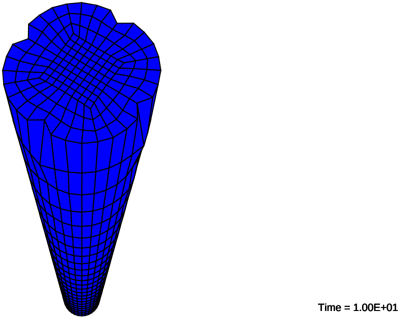

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Summary and Further Work

- 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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Computational Formulation – Some 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 fluxes (Garikipati et al. [2001])
- Large advective terms require stabilization