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


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Growing Tendon Construct

Controlled experiments motivate and validate the descriptive model

- Growth – an addition/loss of mass
- Increasing collagen concentration with age
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- **Growth** – an addition/loss of mass
  - ... *Increasing collagen concentration with age*
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
Arising Issues and Our Current Treatment

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Literature:

- Cowin and Hegedus [1976]
- Kuhl and Steinmann [2002]
- Baaijens et al. [2004]
The Balance of Mass

For collagen: \( \frac{\partial \rho^c_0}{\partial t} = \Pi^c \)

No boundary conditions.
For collagen: \[
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The Balance of Mass

For the fluid: \[ \frac{\partial \rho_f^0}{\partial t} = -\nabla \cdot \mathbf{M}^f \]

Concentration or flux boundary conditions – Tissue exposed to fluid in a bath, fluid injected in at the boundary.
The Balance of Mass

For the fluid: \[ \frac{\partial \rho_f}{\partial t} = -\nabla X \cdot M^f \]

Concentration or flux boundary conditions – *Tissue exposed to fluid in a bath, fluid injected in at the boundary*
The Balance of Mass

For a solute: \[
\frac{\partial \rho_s^0}{\partial t} = \Pi^s - \nabla \chi \cdot M^s
\]

Concentration boundary condition – Tissue exposed to solute in solution in a bath
The Balance of Mass

- For a solute: \( \frac{\partial \rho^s_0}{\partial t} = \Pi^s - \nabla \chi \cdot M^s \)

- Concentration boundary condition – *Tissue exposed to solute in solution in a bath*
The Balance of Momentum

For collagen:
\[ \rho^c_0 \frac{\partial \mathbf{V}}{\partial t} = \rho^c_0 (\mathbf{g} + \mathbf{q}^c) + \nabla_{\mathbf{x}} \cdot \mathbf{P}^c \]
The Balance of Momentum

- Velocity relative to the solid $\mathbf{V}^f = (1/\rho_0^f)\mathbf{FM}^f$
- For the fluid: $\rho_0^f \frac{\partial}{\partial t} (\mathbf{V} + \mathbf{V}^f) = \rho_0^f (g + q^f) + \nabla \cdot \mathbf{P}^f$
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Kinematics of Growth

\[ F = \bar{F}^e \tilde{F}^e \tilde{F}^c \]

Residual stress due to \( \tilde{F}^c \)
Kinematics of Growth

\[ F = \tilde{F}^e \tilde{e}^c \tilde{F}^g c \]

- Residual stress due to \( \tilde{F}^c \)
Constitutive Relations

- Consistent with the dissipation inequality
- Constitutive hypothesis: \( e^t = \hat{e}^t(F^e_t, \rho^t_0, \eta^t) \)

- Collagen Stress: \( P^c = \rho^c_0 \frac{\partial e^c}{\partial F^{ec}} F^{g^c-T} \)
  - Hyperelastic Material
  - Continuum stored energy function based on the Worm-like chain model

- Fluid Stress: \( P^f = \rho^f_0 \frac{\partial e^f}{\partial F^{ef}} F^{g^f-T} \)
  - Ideal Fluid
  - \( \rho^f_0 \hat{e}^f = \frac{1}{2} \kappa (det(F^{ef}) - 1)^2 \), \( \kappa \) – fluid bulk modulus
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Constitutive Relations – Worm-like Chain Model for Collagen

\[ \tilde{\rho}_0^c \hat{e}^c (F^e, \rho_0^c) \]

\[ = \frac{Nk\theta}{4A} \left( \frac{r^2}{2L} + \frac{L}{4(1 - r/L)} - \frac{r}{4} \right) \]

\[ - \frac{Nk\theta}{4\sqrt{2L/A}} \left( \sqrt{\frac{2A}{L}} + \frac{1}{4(1 - \sqrt{2A/L})} - \frac{1}{4} \right) \log(\lambda_1^a \lambda_2^b \lambda_3^c) \]

\[ + \frac{\gamma}{\beta} (J^{e\epsilon} - 2\beta - 1) + 2\gamma \mathbf{1}: \mathbf{E}^e \]

- Embed in Arruda-Boyce Eight Chain Model [1993]

\[ r = \frac{1}{2} \sqrt{a^2 \lambda_1^e + b^2 \lambda_2^e + c^2 \lambda_3^e} \]

- \( \lambda_i^e \) – 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
  \[ M^f = D^f (\rho_0^f F^T g + F^T \nabla (e^f - \theta \eta^f)) \]

- Solute flux (proteins, sugars, nutrients, ...) relative to fluid
  \[ \tilde{V}^s = V^s - V^f \]
  \[ \tilde{M}^s = D^s (\nabla (e^s - \theta \eta^s)) \]

- \( D^f \) and \( D^s \) – Positive semi-definite mobility tensors
Constitutive Relations – Fluxes

- Fluid flux relative to collagen
  \[ M^f = D^f \left( \rho_0^f F^T g + F^T \nabla_X \cdot P^f - \nabla_X (e^f - \theta \eta^f) \right) \]

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Coupled Computations – Examples

- 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: $\Pi^f = -k^f (\rho^f_0 - \rho^f_{0_{ini}})$, $\Pi^c = -\Pi^f$
    - Entropy of mixing: $\eta^f_{mix} = -\frac{k}{\mathcal{M}^f} \log \frac{\rho^f_0}{\rho_0}$
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### Coupled Computations – Examples – Constants

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

- fluid concentration evolution
- fluid sink evolution
- collagen concentration evolution
Coupled Computations – Examples – Swelling

Stress vs Extension Curves

- fluid concentration evolution
- fluid sink evolution
- collagen concentration evolution
Coupled Computations – Examples – Pinching

Before Pinch

After Pinch

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