Computational Modelling of Mechanics and Transport in Growing Tissue

H. Narayanan, K. Garikipati, E. M. Arruda & K. Grosh
University of Michigan

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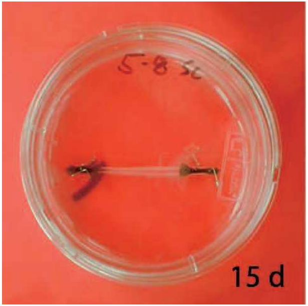
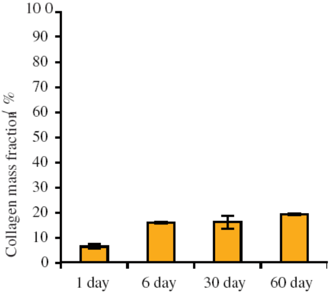
Motivation and definition

Growth/Resorption – An addition or loss of mass



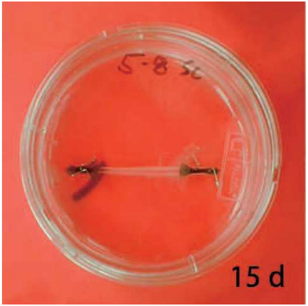
Engineered tendon constructs [Calve et al, 2004]



Increasing collagen concentration with age

Motivation and definition

Growth/Resorption – An addition or loss of mass



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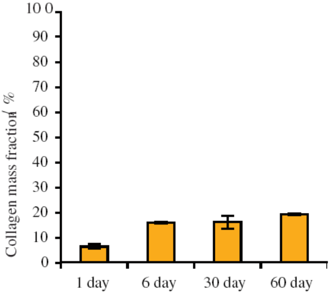

Increasing collagen concentration with age

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
  - Undergoes transport relative to the solid phase
- Dissolved solutes (sugars, proteins, . . .)
  - Undergo transport relative to fluid

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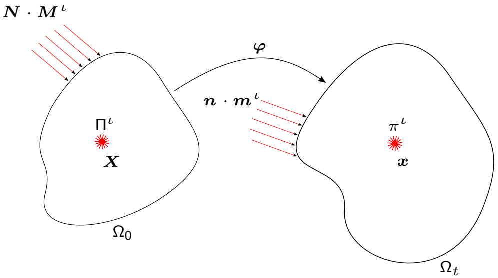
Brief subset of related literature:

- 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]*

Balance of mass



ρ_0^{ι} – Species concentration
Π^{ι} – Species production
$\boldsymbol{M}^{\iota}$ – Species flux

- For a species: $\dfrac{\partial \rho_0^{\iota}}{\partial t} = \Pi^{\iota} - \boldsymbol{\nabla}_X \cdot \boldsymbol{M}^{\iota}$
- Solid – No flux; No boundary conditions
- Fluid – No source; Concentration or flux boundary conditions
- Solute – Flux and source; Concentration boundary condition

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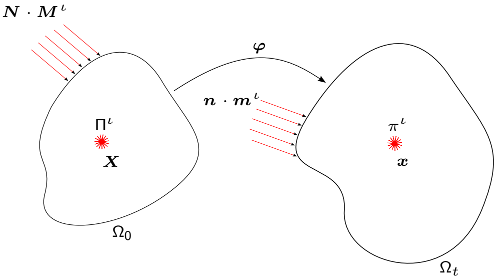

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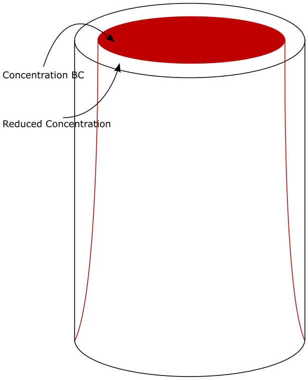
Configuration and physical boundary conditions

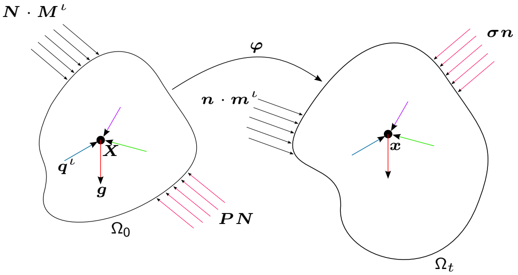


Boundary condition specification

$$\frac{d\rho^i}{dt} + \rho^i \boldsymbol{\nabla}_x \cdot \boldsymbol{v} \; = -\boldsymbol{\nabla}_x \cdot \boldsymbol{m}^i + \pi^i$$

ρ^ι – Current species concentration
π^ι – Current species production
$\boldsymbol{m}^\iota$ – Current species flux
$\boldsymbol{v}$ – Solid velocity

Balance of momentum



ρ_0^{ι} – Species concentration
$\boldsymbol{V}$ – Solid velocity
$\boldsymbol{V}^{\iota}$ – Species relative velocity
$\boldsymbol{g}$ – Body force
$\boldsymbol{q}^{\iota}$ – Interaction force
$\boldsymbol{P}^{\iota}$ – Partial stress

- For a species, velocity relative to the solid: $\boldsymbol{V}^{\iota} = (1/\rho_0^{\iota})\boldsymbol{F}\boldsymbol{M}^{\iota}$

$$\rho_0^{\iota}\frac{\partial}{\partial t}(\boldsymbol{V} + \boldsymbol{V}^{\iota}) = \rho_0^{\iota}(\boldsymbol{g} + \boldsymbol{q}^{\iota}) + \boldsymbol{\nabla}_X \cdot \boldsymbol{P}^{\iota} - (\boldsymbol{\nabla}_X(\boldsymbol{V} + \boldsymbol{V}^{\iota}))\boldsymbol{M}^{\iota}$$

- Negligible contribution to mechanics from dissolved solutes

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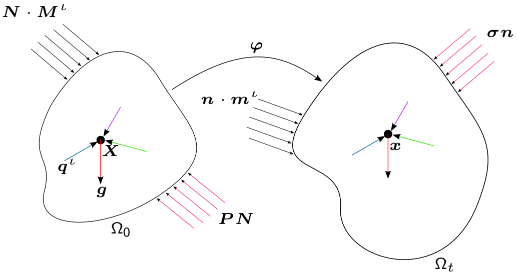

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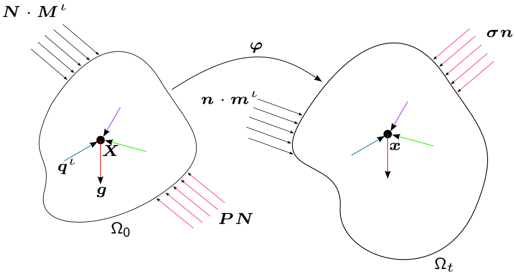

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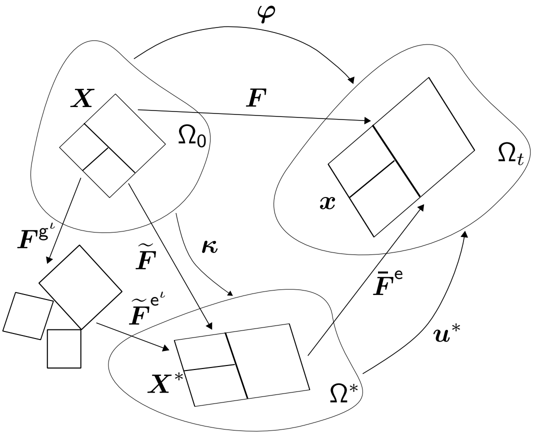
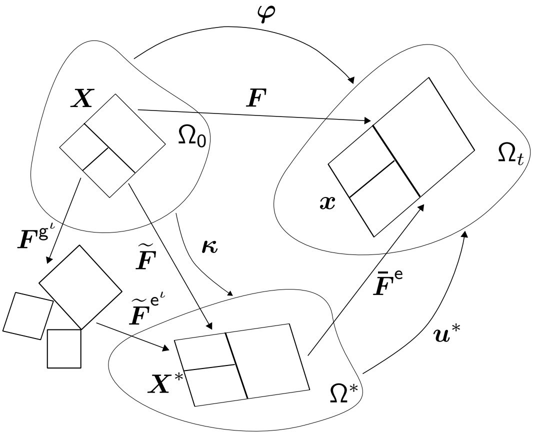
Growth kinematics



- $\boldsymbol{F} = \bar{\boldsymbol{F}}^{\mathrm{e}} \widetilde{\boldsymbol{F}}^{\mathrm{e}^{\iota}} \boldsymbol{F}^{\mathrm{g}^{\iota}}$; $\boldsymbol{F}^{\mathrm{e}^{\iota}} = \bar{\boldsymbol{F}}^{\mathrm{e}} \widetilde{\boldsymbol{F}}^{\mathrm{e}^{\iota}}$; Internal stress due to $\widetilde{\boldsymbol{F}}^{\mathrm{e}^{\iota}}$
- Isotropic swelling due to growth: $\boldsymbol{F}^{\mathrm{g}^{\iota}} = \frac{\rho_0^{\iota}}{\rho_{0_{\mathrm{ini}}}^{\iota}} \mathbf{1}$
- Saturation and swelling

Growth kinematics



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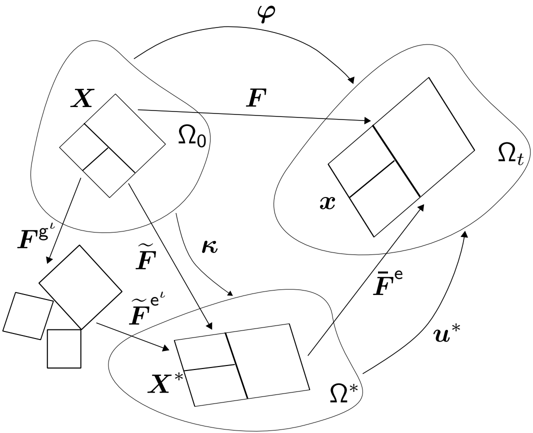

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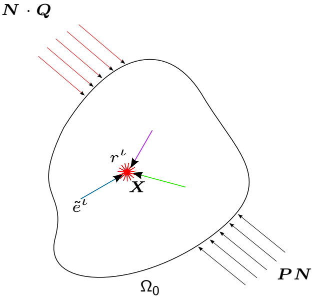
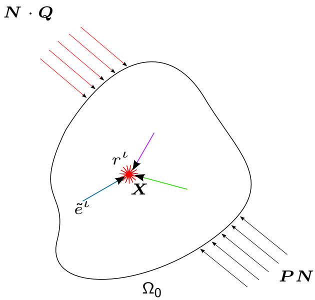
Energy balance and entropy inequality



ρ_0^ι – Species concentration
e^ι – Specific internal energy
$\boldsymbol{P}^\iota$ – Partial stress
$\boldsymbol{F}$ – Deformation gradient
$\boldsymbol{V}^\iota$ – Species relative velocity
$\boldsymbol{Q}^\iota$ – Partial heat flux
r^ι – Species heat supply
$\tilde{e}^\iota$ – Energy transfer
$\boldsymbol{M}^\iota$ – Species flux

$$\rho_0^\iota \frac{\partial e^\iota}{\partial t} = \boldsymbol{P}^\iota : \dot{\boldsymbol{F}} + \boldsymbol{P}^\iota : \boldsymbol{\nabla}_X \boldsymbol{V}^\iota - \boldsymbol{\nabla}_X \cdot \boldsymbol{Q}^\iota + r^\iota + \rho_0^\iota \tilde{e}^\iota - \boldsymbol{\nabla}_X e^\iota \cdot (\boldsymbol{M}^\iota)$$

Energy balance and entropy inequality



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η^ι – Species entropy
θ – Temperature

$$\rho_0^\iota \frac{\partial e^\iota}{\partial t} = \boldsymbol{P}^\iota : \dot{\boldsymbol{F}} + \boldsymbol{P}^\iota : \boldsymbol{\nabla}_X \boldsymbol{V}^\iota - \boldsymbol{\nabla}_X \cdot \boldsymbol{Q}^\iota + r^\iota + \rho_0^\iota \tilde{e}^\iota - \boldsymbol{\nabla}_X e^\iota \cdot (\boldsymbol{M}^\iota)$$

$$\sum_{\iota=\alpha}^{\omega} \rho_0^\iota \frac{\partial \eta^\iota}{\partial t} \geq \sum_{\iota=\alpha}^{\omega} \left(\frac{r^\iota}{\theta} - \boldsymbol{\nabla}_X \eta^\iota \cdot \boldsymbol{M}^\iota - \frac{\boldsymbol{\nabla}_X \cdot \boldsymbol{Q}^\iota}{\theta} + \frac{\boldsymbol{\nabla}_X \theta \cdot \boldsymbol{Q}^\iota}{\theta^2} \right)$$

Constitutive relations for fluxes

- Combine first and second laws to get dissipation inequality
- Constitutive hypothesis $e^\iota = \hat{e}^\iota(\boldsymbol{F}^{\mathsf{e}^\iota}, \rho_0^\iota, \eta^\iota)$
  $\Rightarrow$ Consistent constitutive relations
- Fluid flux relative to collagen
  $$\boldsymbol{M}^f = \boldsymbol{D}^f \left(\rho_0^f \boldsymbol{F}^T \boldsymbol{g} + \boldsymbol{F}^T \boldsymbol{\nabla}_X \cdot \boldsymbol{P}^f - \boldsymbol{\nabla}_X (e^f - \theta \eta^f) \right)$$
- Solute flux (proteins, sugars, nutrients, ...) relative to fluid
  $$\widetilde{\boldsymbol{V}}^s = \boldsymbol{V}^s - \boldsymbol{V}^f$$
  $$\widetilde{\boldsymbol{M}}^s = \boldsymbol{D}^s \left(-\boldsymbol{\nabla}_X (e^s - \theta \eta^s) \right)$$
- $\boldsymbol{D}^f$ and $\boldsymbol{D}^s$ – Positive semi-definite mobility tensors
  Magnitudes from literature, e.g. Mauck et al. [2003]

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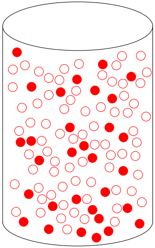
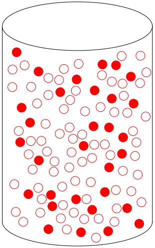
Saturation and Fickian diffusion



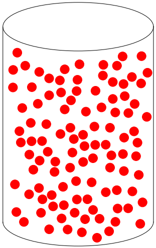
Configuration 1



Configuration 2

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

Saturation and Fickian diffusion

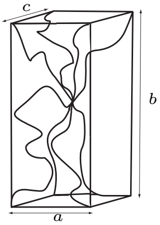


Only possible configuration

- Saturated ⇒ Single configuration ⇒ No Fickian diffusion
- Still have concentration-gradient driven transport due to stress gradient contribution to flux

Worm-like chain model based internal energy density

$$\widetilde{\rho_0}^{\mathsf{c}}\hat{e}^{\mathsf{c}}(\boldsymbol{F}^{\mathsf{e}^{\mathsf{c}}}, \rho_0^{\mathsf{c}})$$



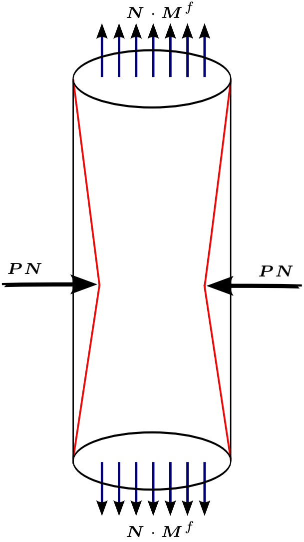
$$\begin{aligned}
&= \frac{Nk\theta}{4A}\left(\frac{r^2}{2L} + \frac{L}{4(1-r/L)} - \frac{r}{4}\right) \\
&- \frac{Nk\theta}{4\sqrt{2L/A}}\left(\sqrt{\frac{2A}{L}} + \frac{1}{4(1-\sqrt{2A/L})} - \frac{1}{4}\right)\log(\lambda_1^{a^2}\lambda_2^{b^2}\lambda_3^{c^2}) \\
&+ \frac{\gamma}{\beta}(J^{\mathsf{e}^{\iota}\,-2\beta}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

- embed in multi chain model [Bischoff et al., 2002]
  $r = \frac{1}{2}\sqrt{a^2\lambda_1^{\mathsf{e}2} + b^2\lambda_2^{\mathsf{e}2} + c^2\lambda_3^{\mathsf{e}2}}$
- λ_I^{e} – elastic stretches along a, b, c
  $\lambda_I^{\mathsf{e}} = \sqrt{\boldsymbol{N}_I \cdot \boldsymbol{C}^{\mathsf{e}}\boldsymbol{N}_I}$

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 fluxes (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 fluid and dissolved nutrient flow $\Rightarrow$ guided tendon growth
- Biphasic model
  - Worm-like chain model for collagen
  - Ideal nearly incompressible fluid $\rho^f \psi^f = \frac{1}{2}\kappa(\det(F^{e^f}) - 1)^2$
- Fluid mobility $D^f_{ij} = 1 \times 10^{-8}\delta_{ij}$, Han et al. [2000]
- First order rate law: $\Pi^{\mathrm{f}} = -k^{\mathrm{f}}(\rho^{\mathrm{f}} - \rho^{\mathrm{f}}_{0_{\mathrm{ini}}}), \quad \Pi^{\mathrm{c}} = -\Pi^{\mathrm{f}}$

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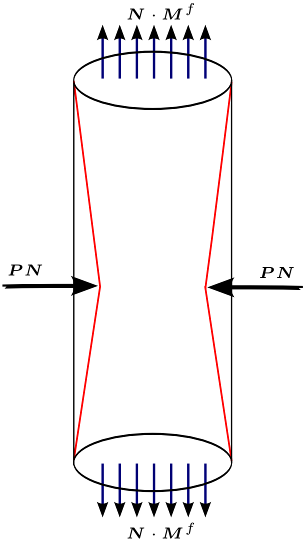

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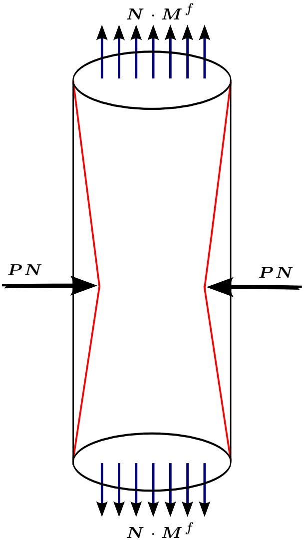

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Results and inferences

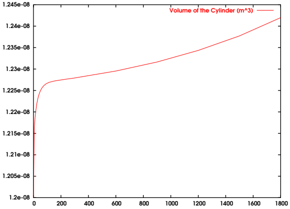
- Total flux in the vertical direction
- Stress driven diffusion

Results and inferences

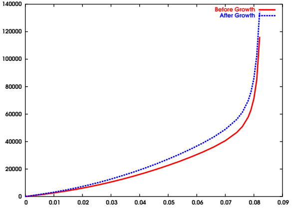
- Regions of high fluid concentration
  $\Rightarrow$ Faster growth
- Relaxation after constriction concludes

Swelling of a tendon immersed in a bath

Volume evolution curve



Stress-extension curves



Collagen concentration evolution

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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