simulations of coupled mechanics and transport in growing soft tissue

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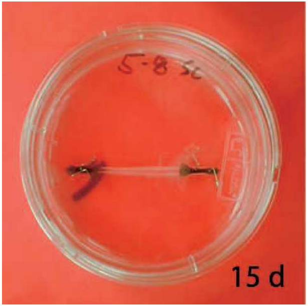
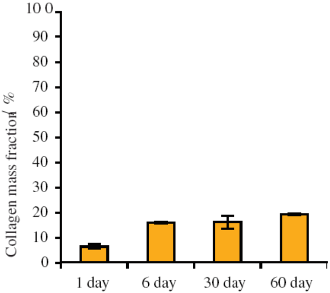
motivation and definition

growth/resorption – an addition or loss of mass



engineered tendon constructs [Calve et al, 2004]



increasing collagen concentration with age

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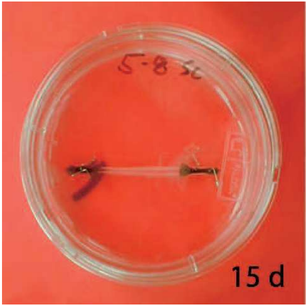

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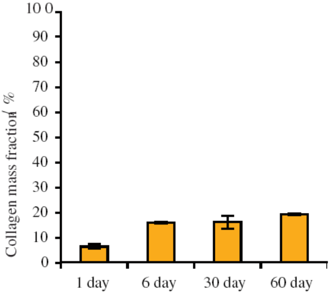

increasing collagen concentration with age

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
  – undergoes transport relative to the solid phase
- dissolved solutes (sugars, proteins, . . .)
  – undergo transport relative to fluid

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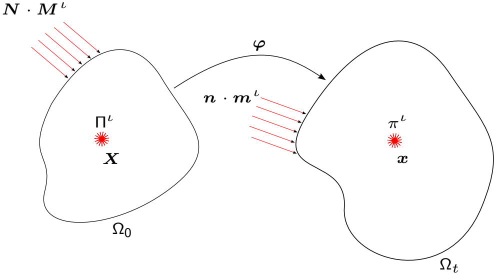
brief subset of related literature:

- 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: $$\frac{\partial \rho_0^{\iota}}{\partial t} = \Pi^{\iota} - \boldsymbol{\nabla}_X \cdot \boldsymbol{M}^{\iota}$$
- 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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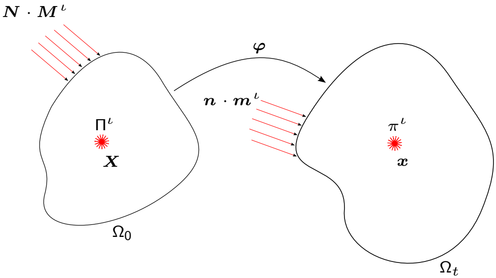

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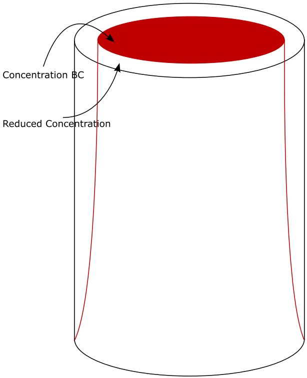
configuration and physical boundary conditions

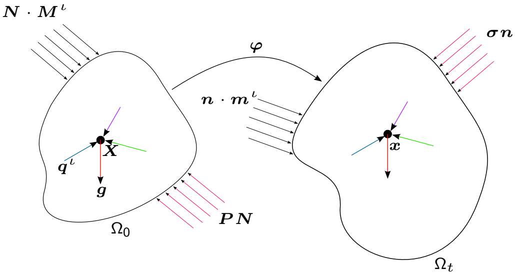


boundary condition specification

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

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

balance of momentum



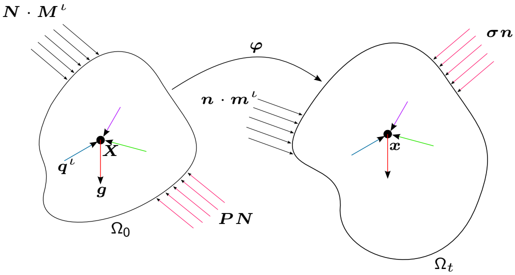
ρ_0^ι – species concentration
V – solid velocity
V^ι – species relative velocity
g – body force
q^ι – interaction force
P^ι – partial stress

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

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

- negligible contribution to mechanics from dissolved solutes

balance of momentum



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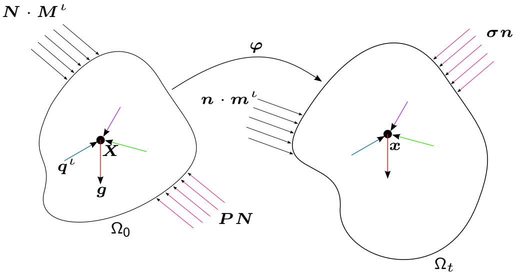

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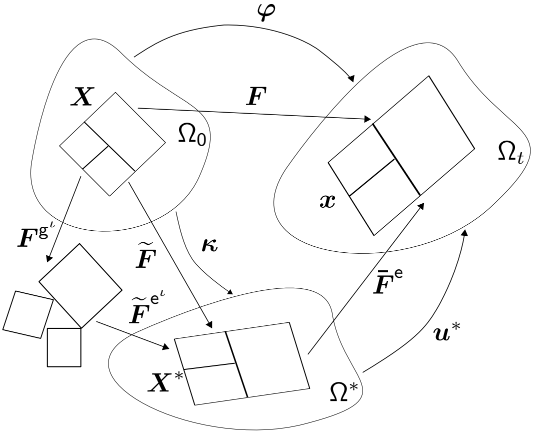
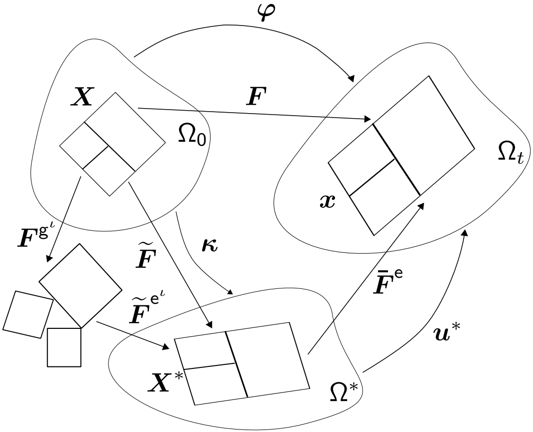
growth kinematics



- $\boldsymbol{F} = \bar{\boldsymbol{F}}^{e} \widetilde{\boldsymbol{F}}^{e^\iota} \boldsymbol{F}^{g^\iota}$; $\boldsymbol{F}^{e^\iota} = \bar{\boldsymbol{F}}^{e} \widetilde{\boldsymbol{F}}^{e^\iota}$; internal stress due to $\widetilde{\boldsymbol{F}}^{e^\iota}$
- isotropic swelling due to growth: $\boldsymbol{F}^{g^\iota} = \frac{\rho_0^\iota}{\rho_{0_{\text{ini}}}^\iota} \boldsymbol{1}$
- saturation and swelling

growth kinematics



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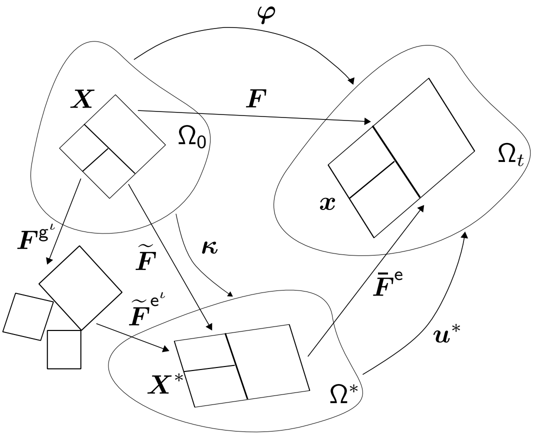

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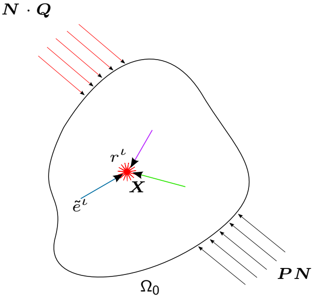
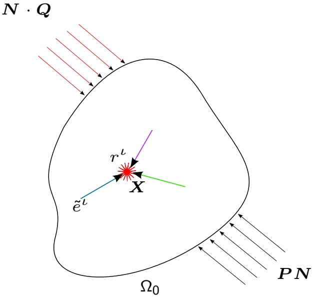
energy balance and entropy inequality



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
  $$\boldsymbol{M}^f = \boldsymbol{D}^f \left(\rho_0^f \boldsymbol{F}^T \boldsymbol{g} + \boldsymbol{F}^T \nabla_X \cdot \boldsymbol{P}^f - \nabla_X (e^f - \theta \eta^f) \right)$$
- solute flux (proteins, sugars, nutrients, ...) relative to fluid
  $$\widetilde{\boldsymbol{V}}^s = \boldsymbol{V}^s - \boldsymbol{V}^f$$
  $$\widetilde{\boldsymbol{M}}^s = \boldsymbol{D}^s \left(-\nabla_X (e^s - \theta \eta^s) \right)$$
- $\boldsymbol{D}^f$ and $\boldsymbol{D}^s$ – positive semi-definite mobility tensors
  magnitudes from literature, e.g. Mauck et al. [2003]

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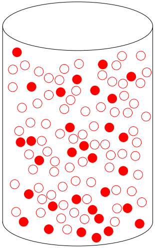
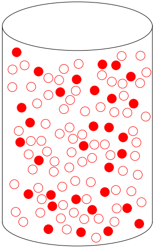
saturation and Fickian diffusion



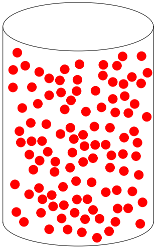
configuration 1



configuration 2

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

saturation and Fickian diffusion

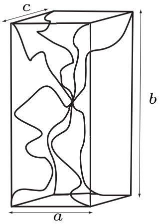


only possible configuration

- saturated $\Rightarrow$ single configuration $\Rightarrow$ 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
  $\lambda_I^{\mathsf{e}} = \sqrt{\boldsymbol{N}_I \cdot \boldsymbol{C}^{\mathsf{e}}\boldsymbol{N}_I}$

some possibilities for sources

- simple first order rate law
  - constituents either “solid” or “fluid”

$$\Pi^{\mathsf{f}} = -k^{\mathsf{f}}(\rho_0^{\mathsf{f}} - \rho_{0_{\mathsf{ini}}}^{\mathsf{f}}), \quad \Pi^{\mathsf{c}} = -\Pi^{\mathsf{f}}$$

- strain energy dependencies
  - weighted by relative densities

$$\Pi^{\mathsf{c}} = \left(\frac{\rho_0^{\mathsf{c}}}{\rho_{0_{\mathsf{ini}}}^{\mathsf{c}}}\right)^{-m} \Psi_0 - \Psi_0^*$$

Harrigan & Hamilton [1993]

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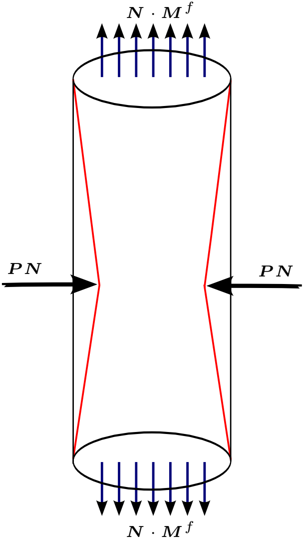
computational formulation details

- 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
- fluid mobility $D^f_{ij} = 1 \times 10^{-8}\delta_{ij}$, Han et al. [2000]
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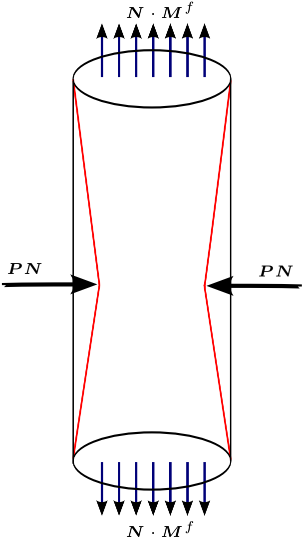

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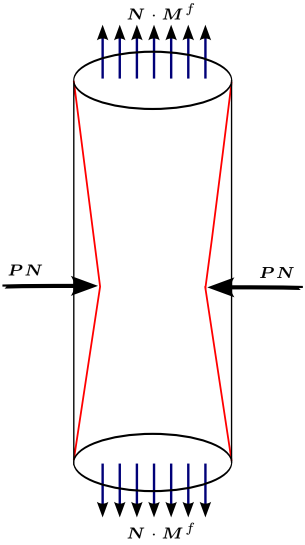

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results and inferences

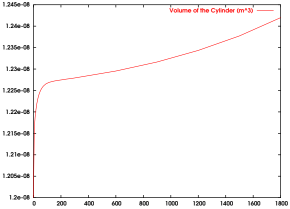
- total flux in the vertical direction
- stress driven diffusion

results and inferences

- regions of high fluid concentration
  $\Rightarrow$ faster growth
- relaxation after constriction concludes

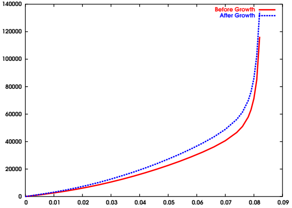
swelling of a tendon immersed in a bath

volume evolution curve



collagen concentration evolution

stress-extension curves



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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