The numerical implications of fluid incompressibility in multiphasic modelling of soft tissue growth

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

Seventh World Congress on Computational Mechanics

July 18th, 2006 – Los Angeles, CA

Recent advances in the physics and mathematics of modelling multiphasic soft tissue growth

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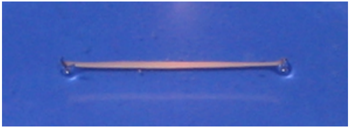
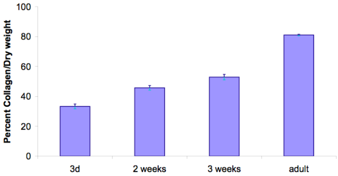
Defining the problem

Growth/Resorption – An addition or loss of mass



Engineered tendon constructs [Calve et al., 2004]



Increasing collagen concentration with age

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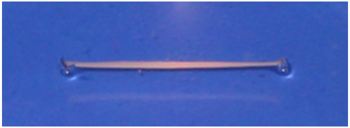

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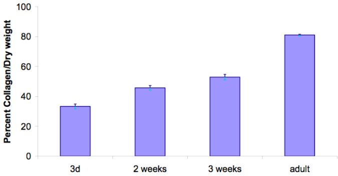
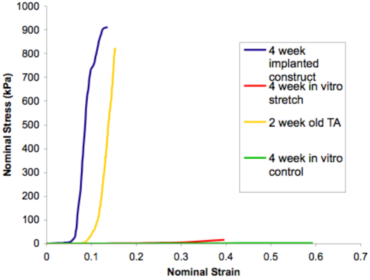


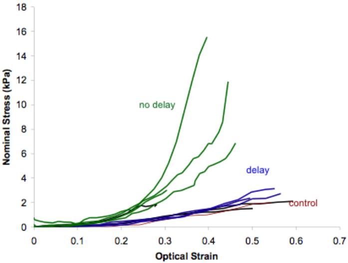
Increasing collagen concentration with age

Open system with multiple species inter-converting and interacting

Factors affecting growth



Chemical environment—Implantation [Calve et al.]



Mechanics—Influence of cyclic load [Calve et al.]

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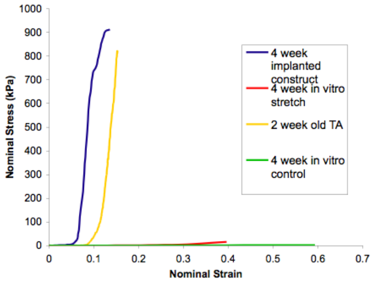

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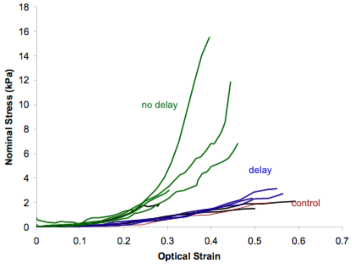

Mechanics—Influence of cyclic load [Calve et al.]

Increase in collagen content and microstructural distribution

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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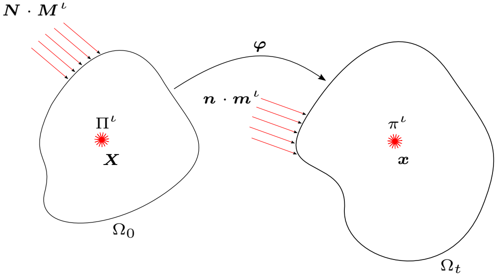
Brief subset of related literature:

- 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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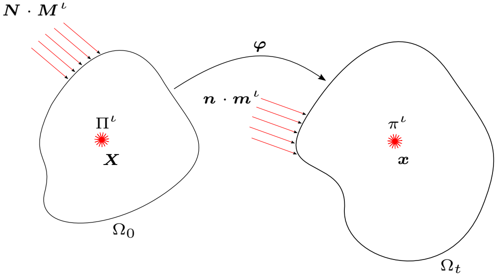

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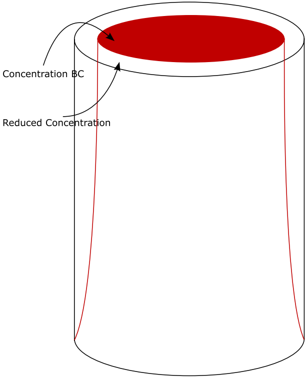
Configuration and physical boundary conditions

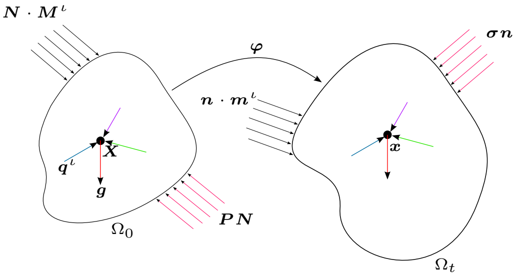


Boundary condition specification

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

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

Balance of momentum



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$\boldsymbol{g}$ – Body force
$\boldsymbol{q}^\iota$ – Interaction force
$\boldsymbol{P}^\iota$ – Partial stress

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

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

- Negligible contribution to mechanics from dissolved solutes

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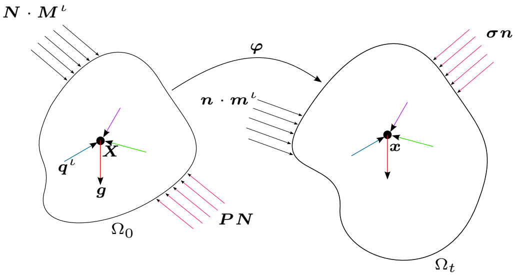

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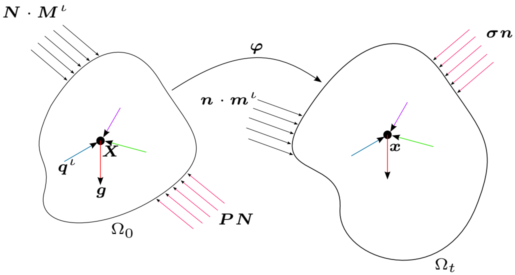

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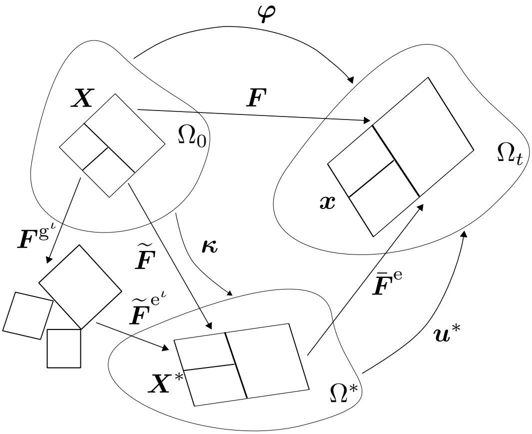
Growth kinematics



- Isotropic swelling due to growth: $\boldsymbol{F}^{\mathrm{g}^\iota} = \left(\frac{\rho^\iota}{\rho^\iota_{0_{\mathrm{ini}}}}\right)^{\frac{1}{3}} \mathbf{1}$
- $\boldsymbol{F} = \bar{\boldsymbol{F}}^{\mathrm{e}} \widetilde{\boldsymbol{F}}^{\mathrm{e}^\iota} \boldsymbol{F}^{\mathrm{g}^\iota}$; $\boldsymbol{F}^{\mathrm{e}^\iota} = \bar{\boldsymbol{F}}^{\mathrm{e}} \widetilde{\boldsymbol{F}}^{\mathrm{e}^\iota}$; Internal stress due to $\widetilde{\boldsymbol{F}}^{\mathrm{e}^\iota}$

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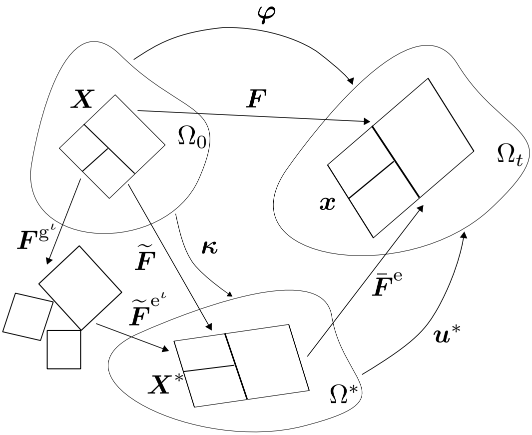

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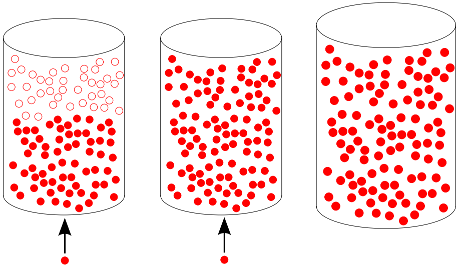
Saturation and swelling



- Pores and tissue begin to swell only after reaching saturation

$$\mathbf{F}^{g^\iota} = \begin{cases} \mathbf{1}, & \sum_\iota v_f^\iota < 1 \\ \left(\frac{\rho_0^\iota}{\rho_{0_{\mathrm{ini}}}^\iota}\right)^{\frac{1}{3}} \mathbf{1}, & \text{otherwise.} \end{cases}$$

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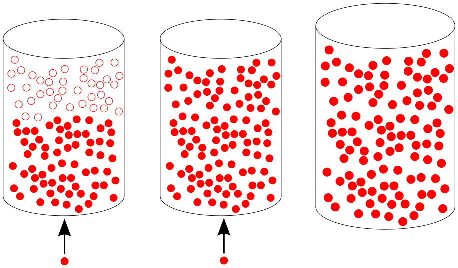

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Constitutive relations

- Combine first and second laws to get dissipation inequality
- Constitutive hypothesis $e^\iota = \hat{e}^\iota(\boldsymbol{F}^{\mathrm{e}^\iota}, \rho_0^\iota, \eta^\iota)$
  $\Rightarrow$ Consistent constitutive relations
- Hyperelastic material law $\boldsymbol{P}^\iota = \rho_0^\iota \frac{\partial e^\iota}{\partial \boldsymbol{F}^{\mathrm{e}^\iota}}$
- 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
  $$\widetilde{\boldsymbol{V}}^s = \boldsymbol{V}^s - \boldsymbol{V}^f$$
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- $\boldsymbol{D}^f$ and $\boldsymbol{D}^s$ – Positive semi-definite mobility tensors
  Magnitudes from literature, e.g. Mauck et al. [2003]

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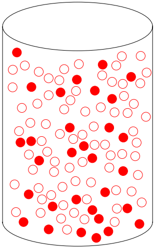
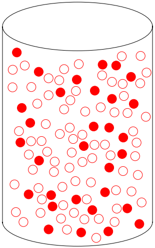
Saturation and Fickian diffusion



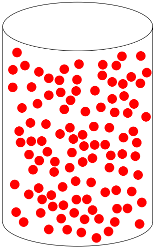
Configuration 1



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

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]
- Backward Euler for time-dependent mass balance
- Mixed method for stress/strain gradient-driven fluxes [Garikipati et al., 2001]
- Large advective terms require stabilisation

Unstable solute transport equation

- Solute transport equation with velocity split $\boldsymbol{V}^{\mathrm{s}} = \widetilde{\boldsymbol{V}}^{\mathrm{s}} + \boldsymbol{V}^{f}$

$$\frac{\mathrm{d}\rho^{\mathrm{s}}}{\mathrm{d}t} = \pi^{\mathrm{s}} - \mathsf{div}\left[\widetilde{\boldsymbol{m}}^{\mathrm{s}} + \frac{\rho^{\mathrm{s}}}{\rho^{f}}\boldsymbol{m}^{f}\right] - \rho^{\mathrm{s}}\mathsf{div}[\boldsymbol{v}]$$

- Advection diffusion equation; Spatial oscillations emerge in numerical solutions at the hyperbolic limit

- Not in a form suitable for standard stabilisation techniques such as SUPG [Hughes et al., 1987]

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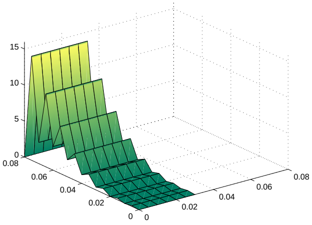

Spatial oscillations using standard Galerkin scheme

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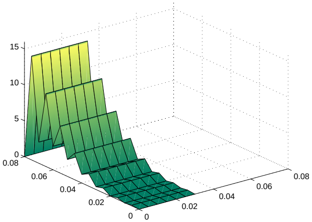

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Implications of fluid incompressibility

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\begin{aligned}
\rho_0^{\mathrm{f}}(\boldsymbol{X},0) &=: \rho^{\mathrm{f}}_{0_{\mathrm{ini}}}(\boldsymbol{X}) \\
&= \rho^{\mathrm{f}}_{\mathrm{ini}}(\boldsymbol{x}\circ\boldsymbol{\varphi})J(\boldsymbol{X},t) \\
&= \frac{\rho^{\mathrm{f}}(\boldsymbol{x}\circ\boldsymbol{\varphi},t)}{J^{f_{\mathrm{g}}}(\boldsymbol{X},t)}J(\boldsymbol{X},t) \\
&= \rho^{\mathrm{f}}(\boldsymbol{x}\circ\boldsymbol{\varphi},t)\cancelto{\approx 1 \text{ for all time } t}{J^{f_{\mathrm{e}}}}(\boldsymbol{X},t)
\end{aligned}
$$

- Incompressibility of the fluid

$$\frac{\partial}{\partial t}\left(\rho^{f}_{0_{\mathrm{ini}}}(\boldsymbol{X})\right) = 0 \Rightarrow \frac{\partial}{\partial t}\left(\rho^{f}(\boldsymbol{x}\circ\boldsymbol{\varphi},t)\right) = 0$$

- Fluid transport equation ($\Pi^{\mathrm{f}} = 0$)

$$0 = \left.\frac{\partial \rho^{f}}{\partial t}\right|_{\boldsymbol{X}} = -\mathrm{div}\left[\rho^{f}\boldsymbol{v}^{f}\right] - \rho^{f}\,\mathrm{div}\left[\boldsymbol{v}\right]$$

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Solute transport reflecting fluid incompressibility

$$\frac{\mathrm{d}\rho^{\mathrm{s}}}{\mathrm{d}t} = \pi^{\mathrm{s}} - \mathsf{div}\left[\widetilde{\boldsymbol{m}^{\mathrm{s}}}\right] - \frac{\boldsymbol{m}^{f} \cdot \mathsf{grad}\left[\rho^{\mathrm{s}}\right]}{\rho^{f}} + \frac{\rho^{\mathrm{s}}\boldsymbol{m}^{f} \cdot \mathsf{grad}\left[\rho^{f}\right]}{{\rho^{f}}^{2}}$$

- Which is of a standard form and is stabilised using SUPG [Hughes, 1987]

$$\frac{\partial \varphi}{\partial t} + \boldsymbol{a} \cdot \mathsf{grad}\left[\varphi\right] = \mathsf{div}\left[\kappa\ \mathsf{grad}\left[\varphi\right]\right] + f$$

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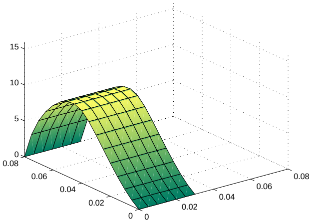
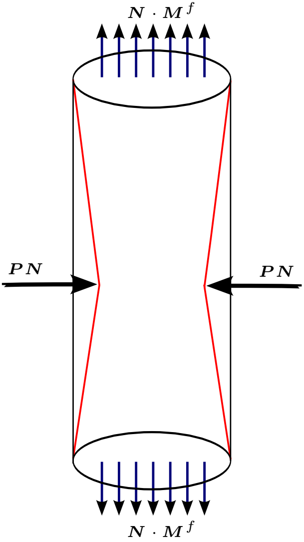


Smooth solutions using SUPG scheme

Example—Nutrient delivery through patch



- Simulating a tendon immersed in a bath
- Constrict it to force fluid and dissolved nutrient flow
- Small nutrient patch on surface
- Triphasic model
  - Worm-like chain model for collagen
  - Ideal, nearly incompressible fluid
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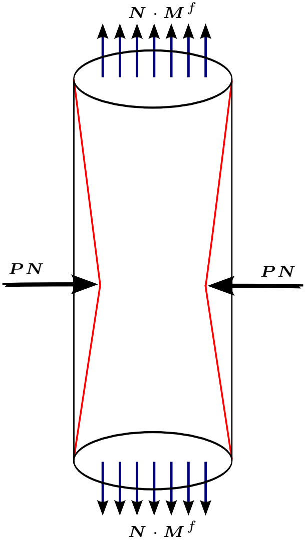

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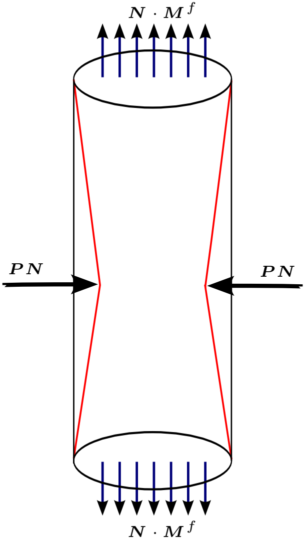

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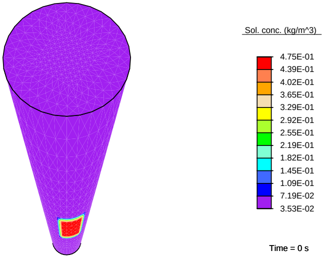
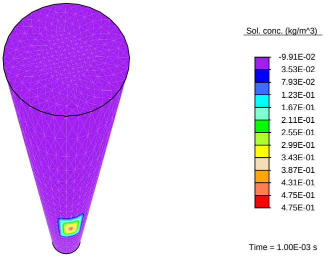
Example—Results and inferences



Patch-like nutrient boundary condition specification



Evolution of solute concentration

Small stress-gradient driven flux; Diffusion dominated

Summary and further work

- Physiologically relevant continuum formulation describing growth in an open system—consistent with mixture theory
- Relevant contributors to growth and healing systematically accounted for—biochemistry, mass transport, coupled mechanics
- Gained insights into the problem
    - The relative roles of these factors
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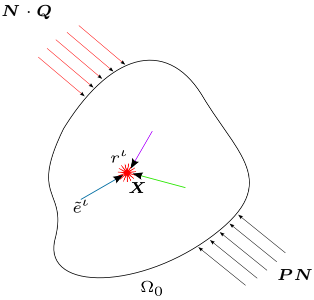
Separator slide

You ought not to be here. Shoo.

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

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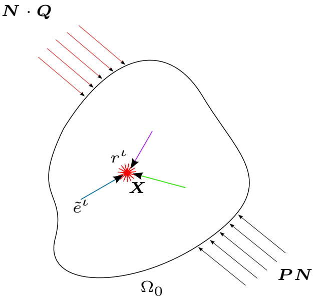

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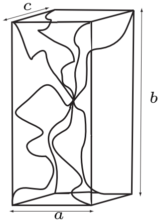
$$\sum_{\iota=\alpha}^{\omega} \rho_0^\iota \frac{\partial \eta^\iota}{\partial t} \geq \sum_{\iota=\alpha}^{\omega} \left(\frac{r^\iota}{\theta} - \boldsymbol{\nabla}_X \eta^\iota \cdot \boldsymbol{M}^\iota - \frac{\boldsymbol{\nabla}_X \cdot \boldsymbol{Q}^\iota}{\theta} + \frac{\boldsymbol{\nabla}_X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

Constitutive relation for mechanics

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



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

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

Possibilities for interconversion laws

- Simple first order rate law –
  Constituents either "solid" or "fluid"

$$\Pi^{\mathrm{f}} = -k^{\mathrm{f}}(\rho^{\mathrm{f}} - \rho^{\mathrm{f}}_{\mathrm{ini}}), \quad \Pi^{\mathrm{c}} = -\Pi^{\mathrm{f}}$$

- Strain Energy Dependencies –
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[Michaelis & Menten, 1913]

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$$\Pi^{\mathrm{c}} = \alpha \Pi^{\mathrm{s}}$$

Enzyme Kinetics

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ES} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

k_1 - Association of substrate and enzyme

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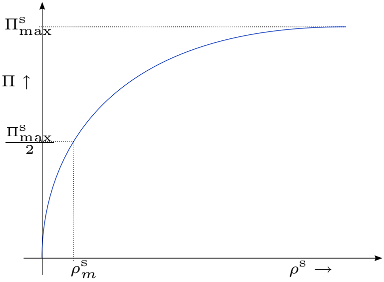

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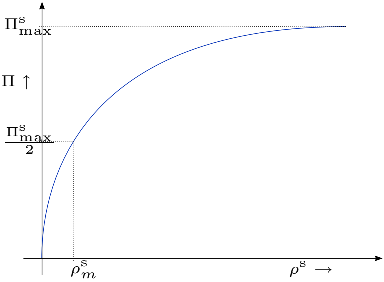

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