

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

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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

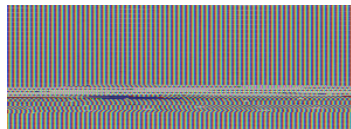
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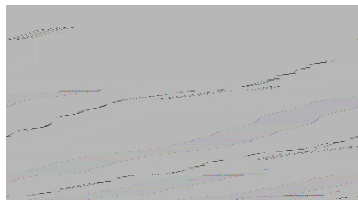
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Defining the problem

Growth/Resorption $\hat{=}$ An addition or loss of mass



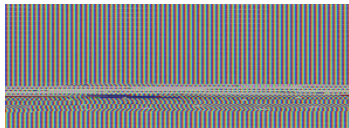
Engineered tendon constructs [Calve et al., 2004]



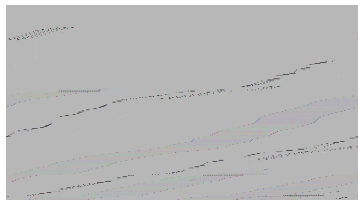
Increasing collagen concentration with age

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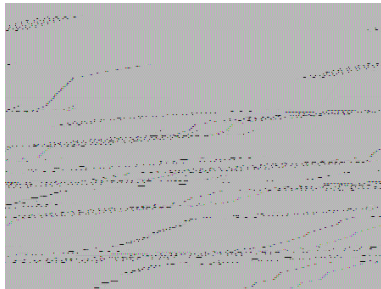
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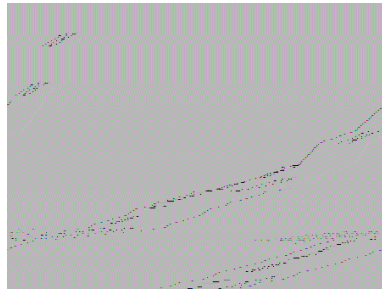
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Open system with multiple species inter-converting and interacting

Factors affecting growth

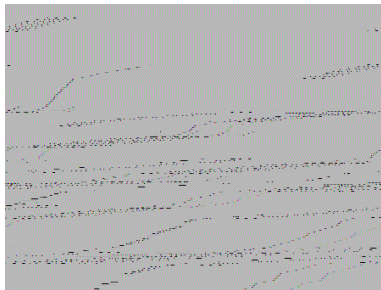


Chemical environment—Implantation [Calve et al.]

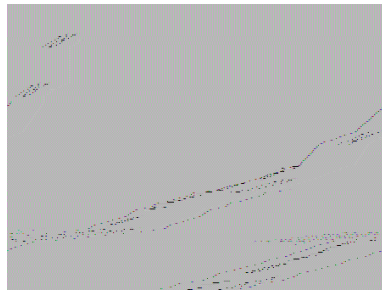


Mechanics—Influence of cyclic load [Calve et al.]

Factors affecting growth



Chemical environment—Implantation [Calve et al.]



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

Modelling approach

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Brief subset of related literature:

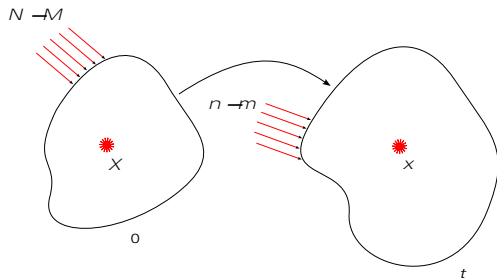
Cowin and Hegedus [1976]

Kuhl and Steinmann [2002]

Sengers, Oomens and Baaijens [2004]

Garikipati et al. – A Journal of the mechanics and physics of solids (52) 1595-1625 [2004]

Balance of mass



x ≡ Species concentration
 \dot{x} ≡ Species production
 M ≡ Species flux

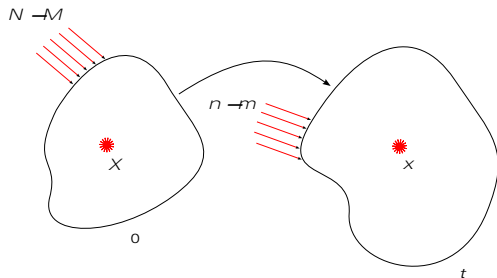
• For a species: $\frac{dQ}{dt} = \dot{x} - M$

• Solid ≡ No flux; No boundary conditions

• Fluid ≡ No source; Concentration or flux boundary conditions

• Solute ≡ Flux and source; Concentration boundary condition

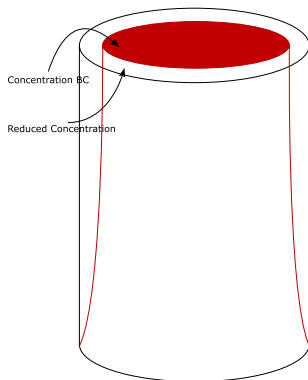
Balance of mass



ρ $\hat{=}$ Species concentration
 $\dot{\rho}$ $\hat{=}$ Species production
 \mathbf{M} $\hat{=}$ Species flux

- For a species: $\frac{\partial \rho}{\partial t} = \dot{\rho} - \nabla \cdot \mathbf{M}$
- Solid $\hat{=}$ No flux; No boundary conditions
- Fluid $\hat{=}$ No source; Concentration or flux boundary conditions
- Solute $\hat{=}$ Flux and source; Concentration boundary condition

Configuration and physical boundary conditions



Boundary condition specification

$$\frac{d c^i}{dt} + c^i \nabla \cdot \mathbf{v} = \dot{c}^i - \nabla \cdot \mathbf{m}^i + \dot{m}^i$$

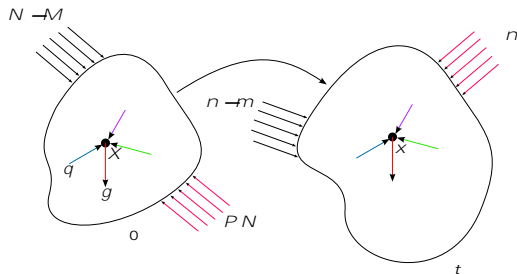
c^i Current species concentration

\dot{c}^i Current species production

\mathbf{m}^i Current species flux

\mathbf{v} Solid velocity

Balance of momentum



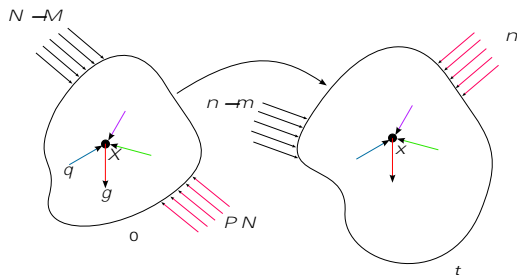
- ρ_0 $\hat{=}$ Species concentration
- V $\hat{=}$ Solid velocity
- V $\hat{=}$ Species relative velocity
- g $\hat{=}$ Body force
- q $\hat{=}$ Interaction force
- P $\hat{=}$ Partial stress

• For a species, velocity relative to the solid: $V = (1/\rho_0) \nabla F M$

$$\rho_0 \nabla \cdot (V + V) = \rho_0 (g + q) + \nabla \cdot P - (\nabla \cdot (V + V)) M$$

• Negligible contribution to mechanics from dissolved solutes

Balance of momentum



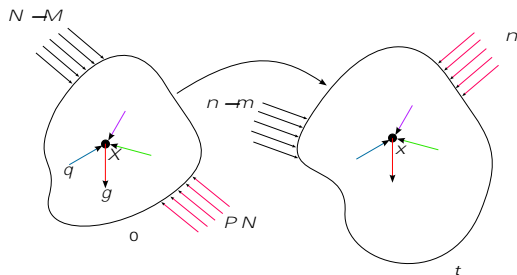
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• For a species, velocity relative to the solid: $\mathbf{V} = (1/\rho_0)\mathbf{F}\mathbf{M}$

$$\rho_0 \frac{d}{dt} (\mathbf{V} + \mathbf{V}) = \rho_0 (\mathbf{g} + \mathbf{q}) + \mathbf{x} \cdot \mathbf{P} - (\mathbf{x} \cdot (\mathbf{V} + \mathbf{V})) \mathbf{M}$$

• Negligible contribution to mechanics from dissolved solutes

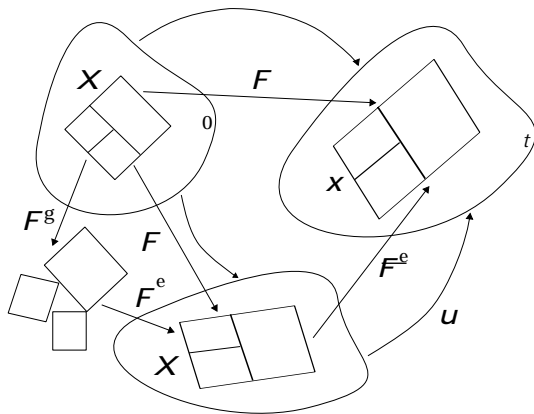
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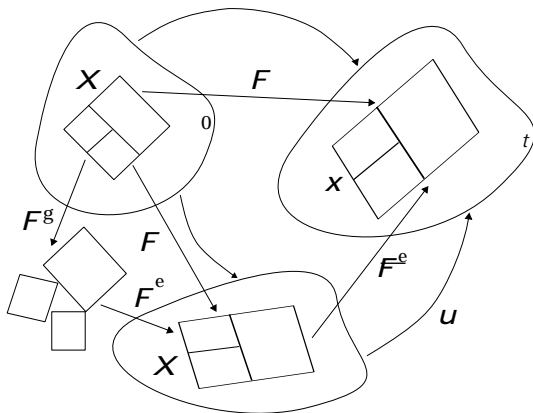
Growth kinematics



• Isotropic swelling due to growth: $F^g = \frac{1}{\lambda_{ini}^3} \mathbf{1}$

• $F = F^g F^e$; $F^e = F F^g$; Internal stress due to F^g

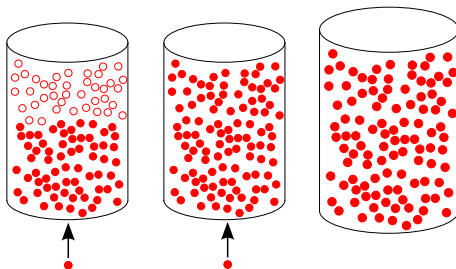
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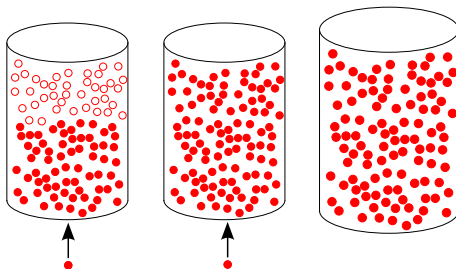
Saturation and swelling



- Pores and tissue begin to swell only after reaching saturation

$$F^0 = \begin{cases} 1, & v_F < 1 \\ \frac{\phi}{\phi_{\text{ini}}} \frac{1}{3}, & \text{otherwise.} \end{cases}$$

Saturation and swelling



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$$F^g = \begin{cases} 1, & V_f < 1 \\ \frac{0}{0_{\text{ini}}} \frac{1}{3}, & \text{otherwise.} \end{cases}$$

Constitutive relations

- Combine first and second laws to get dissipation inequality
- Constitutive hypothesis $e = \hat{e}(\mathbf{F}^e, \theta, \dots)$
Consistent constitutive relations

- Hyperelastic material law $\mathbf{P} = \frac{\partial e}{\partial \mathbf{F}^e}$

- Fluid flux relative to collagen

$$\mathbf{M}^f = \mathbf{D}^f \left(\frac{\partial e}{\partial \mathbf{F}^f} \mathbf{F}^T \mathbf{g} + \mathbf{F}^T \right) \chi - \mathbf{P}^f \dot{\chi} = \chi (\mathbf{e}^f - \mathbf{e}^f)$$

- Solute flux (proteins, sugars, nutrients, ...) relative to fluid

$$\mathbf{V}^s = \mathbf{V}^s - \mathbf{V}^f$$
$$\mathbf{M}^s = \mathbf{D}^s \left(\dot{\chi} - \chi (\mathbf{e}^s - \mathbf{e}^s) \right)$$

- \mathbf{D}^f and \mathbf{D}^s Positive semi-definite mobility tensors

Magnitudes from literature, e.g. Mauck et al. [2003]

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- Solute flux (proteins, sugars, nutrients, ...) relative to fluid

$$\mathbf{V}^s = \mathbf{V}^s - \mathbf{V}^f$$

$$\mathbf{M}^s = \mathbf{D}^s \left(-\chi (e^s - e^f) \right)$$

- \mathbf{D}^f and \mathbf{D}^s : Positive semi-definite mobility tensors

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$$\mathbf{M}^f = \mathbf{D}^f \left(\frac{f}{\theta} \mathbf{F}^T \mathbf{g} + \mathbf{F}^T \right) \times -\mathbf{P}^f \dot{\epsilon} \quad \times (e^f \dot{\epsilon} - \dot{f})$$

- Solute flux (proteins, sugars, nutrients, ...) relative to fluid

$$\mathbf{V}^s = \mathbf{V}^s \dot{\epsilon} - \mathbf{V}^f$$

$$\mathbf{M}^s = \mathbf{D}^s \left(\dot{\epsilon} - \frac{1}{\theta} \times (e^s \dot{\epsilon} - \dot{s}) \right)$$

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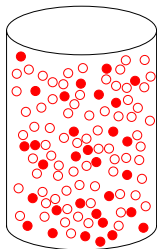
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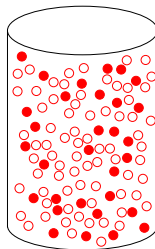
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Saturation and Fickian diffusion



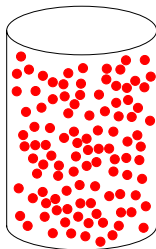
Configuration 1



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 $\mathbf{V}^s = \mathbf{V}^s + \mathbf{V}^f$

$$\frac{d^s}{dt} = \mathbf{v}^s \cdot \text{div} \mathbf{m}^s + \frac{\mathbf{v}^s}{f} \mathbf{m}^f \cdot \text{div}[\mathbf{v}]$$

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

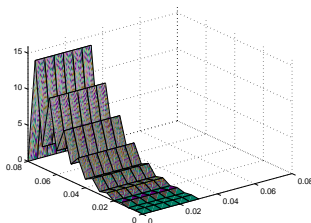
- Not in a form suitable for standard stabilisation techniques such as SUPG [Hughes et al., 1987]

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Spatial oscillations using standard Galerkin scheme

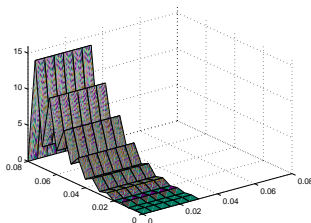
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Implications of fluid incompressibility

$$\begin{aligned}
 f_0(\mathbf{X}, 0) &=: f_{0\text{ini}}(\mathbf{X}) \\
 &= f_{\text{ini}}(\mathbf{x}) J(\mathbf{X}, t) \\
 &= \frac{f(\mathbf{x}, t)}{J^{f_g}(\mathbf{X}, t)} J(\mathbf{X}, t) \\
 &= f(\mathbf{x}, t) J^{f_e}(\mathbf{X}, t) \quad 1 \text{ for all time } t
 \end{aligned}$$

• Incompressibility of the fluid

$$\frac{d}{dt} f_{0\text{ini}}(\mathbf{X}) = 0 \quad \frac{d}{dt} f(\mathbf{x}, t) = 0$$

• Fluid transport equation ($f = 0$)

$$0 = \frac{d}{dt} f = \frac{d}{dt} \int_{\mathbf{X}} f = \int_{\mathbf{X}} \frac{d}{dt} f = \int_{\mathbf{X}} \text{div} [f \mathbf{v}] = \int_{\mathbf{X}} \text{div} [f \mathbf{v}]$$

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$$0 = \frac{df}{dt} \mathbf{X} = -\text{div} \left(f \mathbf{v}^f \right) - f \text{div} [\mathbf{v}]$$

Solute transport reflecting fluid incompressibility

$$\frac{d^s}{dt} = \frac{1}{f} \left(\frac{d^f}{dt} - \text{div} \left(m^s \frac{1}{f} \right) - \frac{m^f \cdot \text{grad} \left(\frac{1}{f} \right)}{f} \right) + \frac{m^f \cdot \text{grad} \left(\frac{1}{f} \right)}{f^2}$$

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

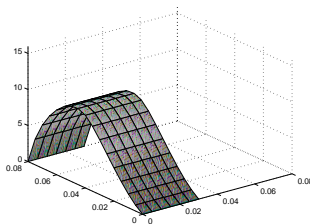
$$\frac{d^s}{dt} + a \cdot \text{grad} \left(\frac{1}{f} \right) = \text{div} \left(\frac{1}{f} \text{grad} \left(\frac{1}{f} \right) \right) + f$$

Solute transport reflecting fluid incompressibility

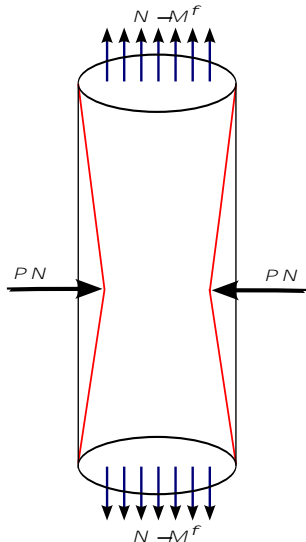
$$\frac{d^s}{dt} = \frac{1}{f} \left(\frac{d^f}{dt} - \text{div} [m^s] - \frac{m^f \text{grad} [^s]}{f} + \frac{^s m^f \text{grad} ^f}{f^2} \right)$$

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Example—Nutrient delivery through patch



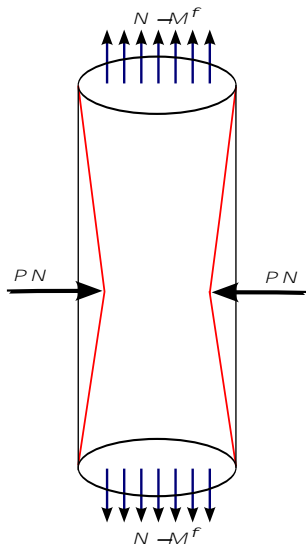
- Simulating a tendon immersed in a bath
- Constrict it to force fluid and dissolved nutrient flow
- Small nutrient patch on surface

• Triphasic model

- Fluid mobility [Han et al., 2000]
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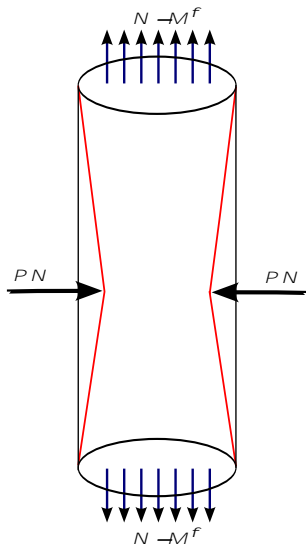


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 - Worm-like chain model for collagen
 - Ideal, nearly incompressible fluid
 - Enzyme kinetics for inter-conversion

• Fluid mobility [Han et al., 2000]

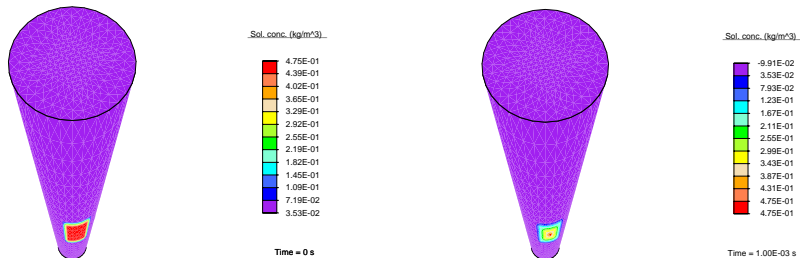
Solute mobility [Mauck et al., 2003]

Example—Nutrient delivery through patch



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 - Ideal, nearly incompressible fluid
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- Fluid mobility [Han et al., 2000]
Solute mobility [Mauck et al., 2003]

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
 - Influence of saturation on growth and diffusion
 - Configuration choice and physical boundary conditions
 - The kinematics challenges involved
- Revisit basic kinematic assumptions to enhance model

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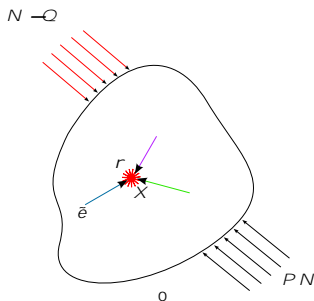
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Separator slide

You ought not to be here. Shoo.

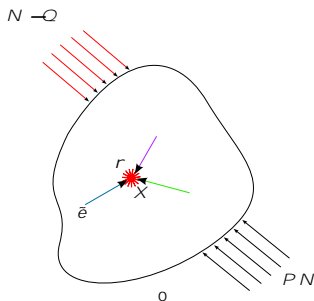
Energy balance and entropy inequality



- ρ $\hat{=}$ Species concentration
- e $\hat{=}$ Specific internal energy
- \mathbf{P} $\hat{=}$ Partial stress
- \mathbf{F} $\hat{=}$ Deformation gradient
- \mathbf{V} $\hat{=}$ Species relative velocity
- \mathbf{Q} $\hat{=}$ Partial heat flux
- r $\hat{=}$ Species heat supply
- \bar{e} $\hat{=}$ Energy transfer
- \mathbf{M} $\hat{=}$ Species flux

$$\rho \frac{de}{dt} = \mathbf{P} : \dot{\mathbf{F}} + \mathbf{P} : \mathbf{x} \mathbf{V} \hat{=} \mathbf{x} \cdot \mathbf{Q} + r + \rho \bar{e} \hat{=} \mathbf{x} \cdot \mathbf{e} - (\mathbf{M})$$

Energy balance and entropy inequality



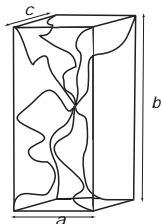
- ρ_0 $\hat{=}$ Species concentration
- e $\hat{=}$ Specific internal energy
- P $\hat{=}$ Partial stress
- F $\hat{=}$ Deformation gradient
- V $\hat{=}$ Species relative velocity
- Q $\hat{=}$ Partial heat flux
- r $\hat{=}$ Species heat supply
- \bar{e} $\hat{=}$ Energy transfer
- M $\hat{=}$ Species flux
- η $\hat{=}$ Species entropy
- θ $\hat{=}$ Temperature

$$\rho_0 \frac{de}{dt} = P : \dot{F} + P : \nabla_x V \hat{=} \nabla_x \cdot Q + r + \rho_0 \bar{e} \hat{=} \nabla_x \cdot e - (M)$$

$$= \rho_0 \frac{de}{dt} = \nabla_x \cdot M \hat{=} \frac{\nabla_x \cdot Q}{\theta} + \frac{\nabla_x \cdot Q}{\theta^2}$$

Constitutive relation for mechanics

$$\sigma^c \partial^c (F^{e^c}, \epsilon_0^c)$$



$$\begin{aligned} &= \frac{Nk}{4A} \frac{r^2}{2L} + \frac{L}{4(1 - r/L)} - \frac{r}{4} \\ &- \frac{Nk}{4} \frac{\overline{2A}}{2L/A} + \frac{1}{4(1 - \frac{1}{2A/L})} - \frac{1}{4} \log\left(\frac{a^2}{1} \frac{b^2}{2} \frac{c^2}{3}\right) \\ &+ \frac{1}{2} (J^e - 1) + \frac{1}{2} E^{e^c} \end{aligned}$$

- Embed in multi chain model [Bischoff et al., 2002]

$$r = \frac{1}{2} \left(a^2 \frac{e_1^2}{1} + b^2 \frac{e_2^2}{2} + c^2 \frac{e_3^2}{3} \right)$$

- e_i - elastic stretches along a, b, c

$$e_i = \frac{N_i - \epsilon^e N_i}{N_i}$$

Possibilities for interconversion laws

- Simple first order rate law \dot{c}
Constituents either "solid" or "fluid"

$$\dot{f} = -k^f (f - f_{ini}), \quad \dot{c} = -\dot{f}$$

- Strain Energy Dependencies \dot{c}
Weighted by relative densities

$$\dot{c} = \frac{1}{\rho} \sum_i \rho_i \frac{\partial \psi}{\partial \epsilon_i} \epsilon_i$$

(Gurtin & Murdoch, 1975)

- Enzyme Kinetics \dot{c} Introducing
additional species to the mixture

$$\dot{c} = \frac{1}{\rho} \sum_i \rho_i \frac{\partial \psi}{\partial \epsilon_i} \epsilon_i$$

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- Cell Signalling \dot{c} Preferential growth in
damaged regions

Possibilities for interconversion laws

- Simple first order rate law \dot{c}
Constituents either "solid" or "fluid"

$$\dot{f} = -k^f (f - f_{ini}), \quad \dot{c} = -c f$$

- Strain Energy Dependencies \dot{c}
Weighted by relative densities

$$\dot{c} = \left(\frac{c}{c_{0ini}} \right)^{-m} \dot{\epsilon} - \dot{\epsilon} c$$

[Harrigan & Hamilton, 1993]

- Enzyme Kinetics \dot{c} Introducing additional species to the mixture
- Polymerization \dot{c} Polymerization
- Cell Signalling \dot{c} Preferential growth in damaged regions

Possibilities for interconversion laws

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

$$f = k^f (f_{ini} - f), \quad c = f$$

- Strain Energy Dependencies –
Weighted by relative densities

$$c = \left(\frac{c}{c_{ini}} \right)^m \quad 0 < m < 1$$

[Harrigan & Hamilton, 1993]

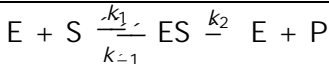
- Enzyme Kinetics – Introducing additional species to the mixture

$$s = \frac{s_{max}}{s_m + s} \quad \text{cell}, \quad c = s$$

[Michaelis & Menten, 1913]

- Cell Signalling – Preferential growth in damaged regions

Enzyme Kinetics

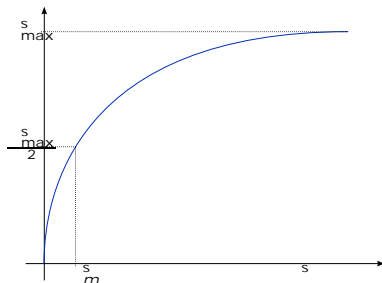


k_1 - Association of substrate and enzyme

k_{-1} - Dissociation of unaltered substrate

k_2 - Formation of product

$$s_m = \frac{(k_2 + k_{-1})}{k_1}$$



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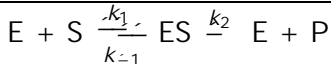
$$s = \frac{(s_{max} - s)}{(s_m + s)} \quad \text{cell}, \quad c = s$$

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- Cell Signalling – Preferential growth in damaged regions

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Enzyme Kinetics

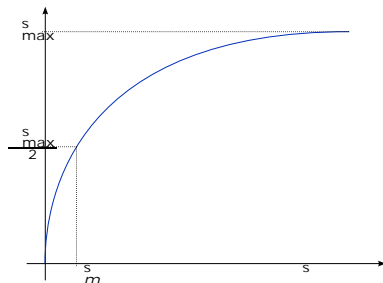


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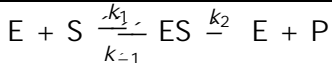
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