

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

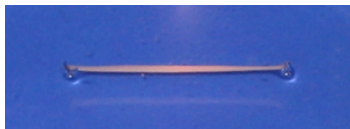
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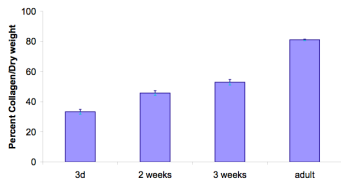
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Defining the problem

Growth/Resorption – An addition or loss of mass



Engineered tendon constructs [Calve et al., 2004]



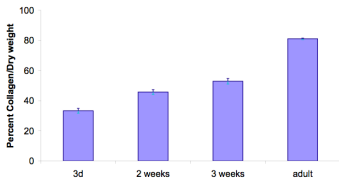
Increasing collagen concentration with age

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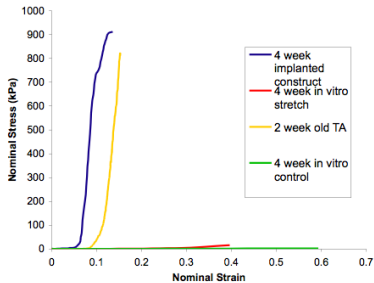
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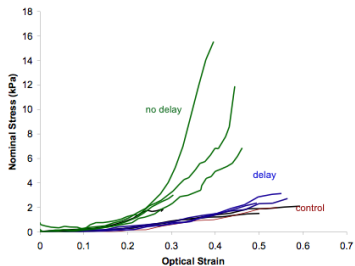
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Open system with multiple species inter-converting and interacting

Factors affecting growth

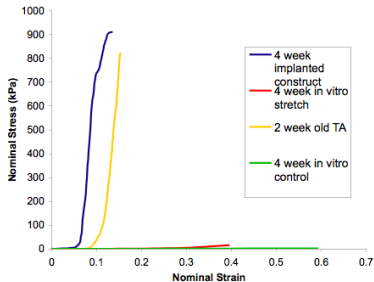


Chemical environment—Implantation [Calve et al.]

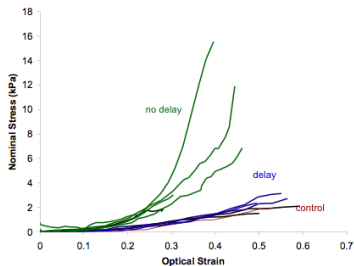


Mechanics—Influence of cyclic load [Calve et al.]

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

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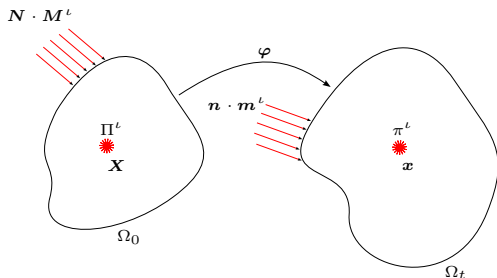
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Brief subset of related literature:

- 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]*

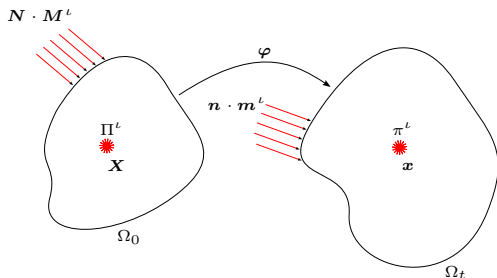
Balance of mass



ρ_0^l – Species concentration
 Π^l – Species production
 M^l – Species flux

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

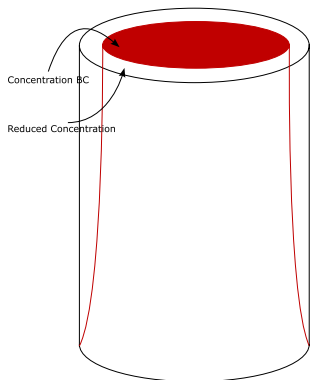
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Configuration and physical boundary conditions



Concentration BC

Reduced Concentration

Boundary condition specification

$$\frac{d\rho^i}{dt} + \rho^i \nabla_x \cdot \mathbf{v} = -\nabla_x \cdot \mathbf{m}^i + \pi^i$$

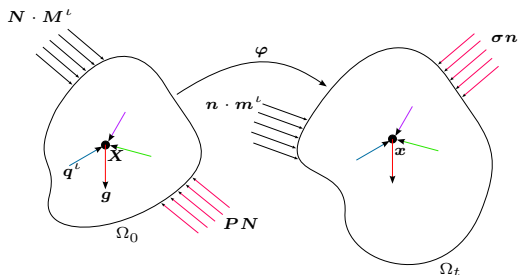
ρ^i – Current species concentration

π^i – Current species production

\mathbf{m}^i – Current species flux

\mathbf{v} – Solid velocity

Balance of momentum



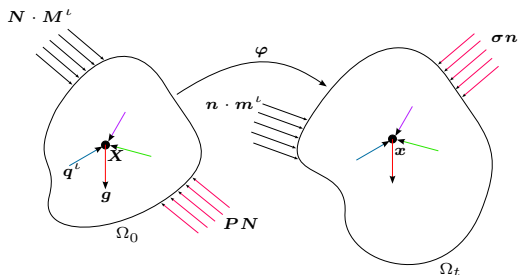
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 V – Solid velocity
 V^l – Species relative velocity
 g – Body force
 q^l – Interaction force
 P^l – Partial stress

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

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

- Negligible contribution to mechanics from dissolved solutes

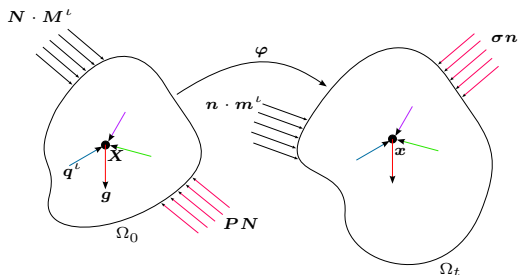
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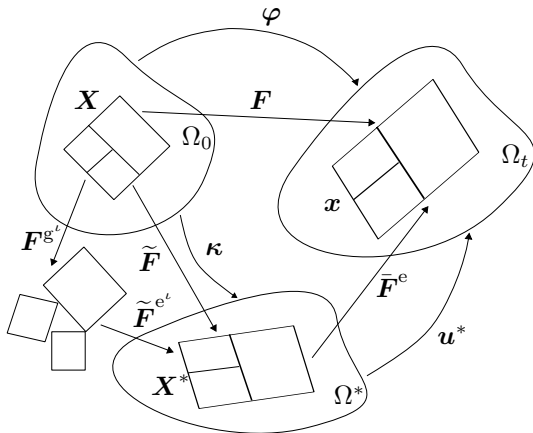
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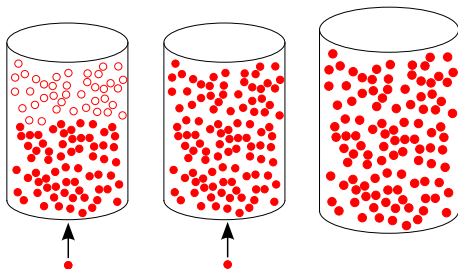
Growth kinematics



- Isotropic swelling due to growth: $F^{g^t} = \left(\frac{\rho^t}{\rho_{0\text{ini}}^t} \right)^{\frac{1}{3}} \mathbf{1}$

• $F = \bar{F}^e \tilde{F}^{e^t} F^{g^t}$; $F^{g^t} = \bar{F}^e \tilde{F}^{e^t}$; Internal stress due to \tilde{F}^{e^t}

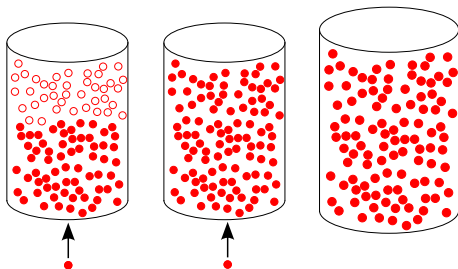
Saturation and swelling



- Pores and tissue begin to swell only after reaching saturation

$$Fg' = \begin{cases} 1, & \sum_i v_f' < 1 \\ \left(\frac{\rho_b'}{\rho_{b_{\text{ini}}}} \right)^{\frac{1}{3}}, & \text{otherwise.} \end{cases}$$

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Constitutive relations

- Combine first and second laws to get dissipation inequality
- Constitutive hypothesis $e^l = \hat{e}^l(\mathbf{F}^{e^l}, \rho_0^l, \eta^l)$
⇒ Consistent constitutive relations

- Hyperelastic material law $\mathbf{P}^l = \rho_0^l \frac{\partial e^l}{\partial \mathbf{F}^l}$

- Fluid flux relative to collagen

$$\mathbf{M}^f = \mathbf{D}^f \left(\rho_0^f \mathbf{F}^{Tf} \mathbf{g} + \mathbf{F}^{Tf} \nabla_X \cdot \mathbf{P}^f - \nabla_X (e^f - \theta \eta^f) \right)$$

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

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

$$\tilde{\mathbf{M}}^s = \mathbf{D}^s (-\nabla_X (e^s - \theta \eta^s))$$

- \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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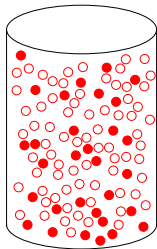
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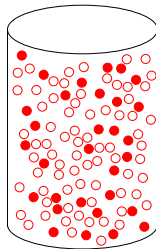
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Saturation and Fickian diffusion



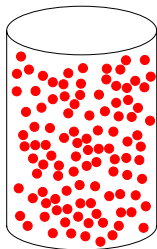
Configuration 1



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 \Rightarrow Single configuration \Rightarrow 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 $\mathbf{V}^s = \widetilde{\mathbf{V}}^s + \mathbf{V}^f$

$$\frac{d\rho^s}{dt} = \pi^s - \operatorname{div} \left[\widetilde{\mathbf{m}}^s + \frac{\rho^s}{\rho^f} \mathbf{m}^f \right] - \rho^s \operatorname{div}[\mathbf{v}]$$

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

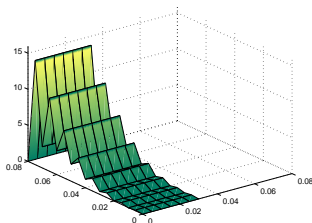
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Spatial oscillations using standard Galerkin scheme

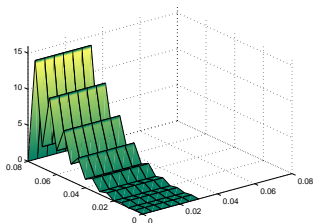
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Implications of fluid incompressibility

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

- Incompressibility of the fluid

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

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Solute transport reflecting fluid incompressibility

$$\frac{d\rho^s}{dt} = \pi^s - \operatorname{div} [\widetilde{\mathbf{m}}^s] - \frac{\mathbf{m}^f \cdot \operatorname{grad} [\rho^s]}{\rho^f} + \frac{\rho^s \mathbf{m}^f \cdot \operatorname{grad} [\rho^f]}{\rho^{f^2}}$$

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

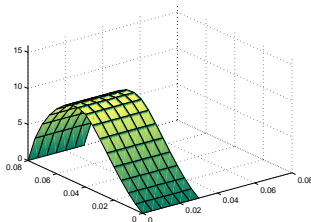
$$\frac{\partial \varphi}{\partial t} + \mathbf{a} \cdot \operatorname{grad} [\varphi] = \operatorname{div} [\kappa \operatorname{grad} [\varphi]] + f$$

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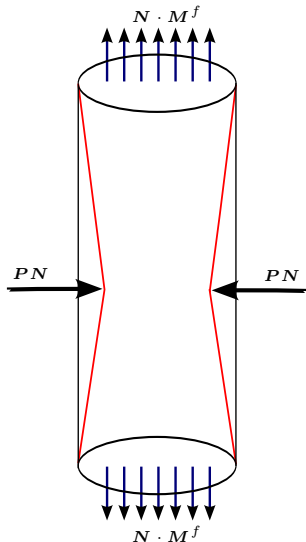
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Example—Nutrient delivery through patch

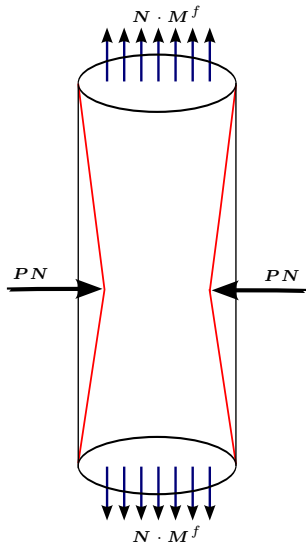


- Simulating a tendon immersed in a bath
- Constrict it to force fluid and dissolved nutrient flow
- Small nutrient patch on surface

- Triphasic model

- Fluid mobility [Han et al., 2000]
- Solute mobility [Mauck et al., 2003]

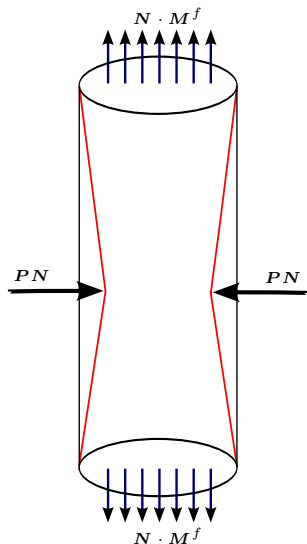
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 - Worm-like chain model for collagen
 - Ideal, nearly incompressible fluid
 - Enzyme kinetics for inter-conversion

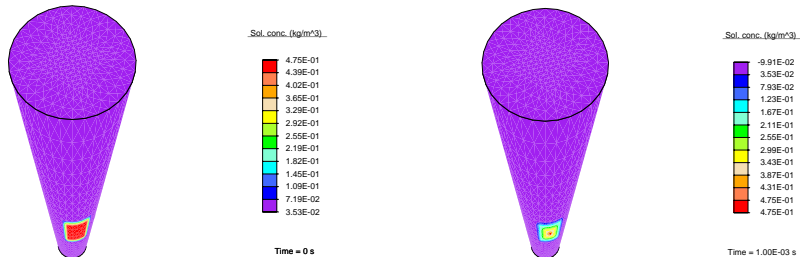
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- Fluid mobility [Han et al., 2000]
Solute mobility [Mauck et al., 2003]

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
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 - The kinematics challenges involved
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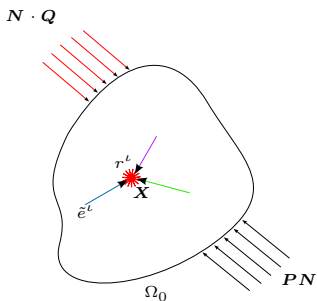
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Separator slide

You ought not to be here. Shoo.

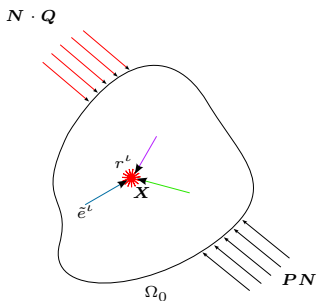
Energy balance and entropy inequality



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

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

Energy balance and entropy inequality



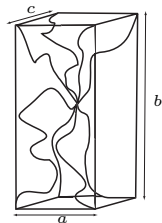
- ρ_0^ℓ – Species concentration
- e^ℓ – Specific internal energy
- P^ℓ – Partial stress
- F – Deformation gradient
- V^ℓ – Species relative velocity
- Q^ℓ – Partial heat flux
- r^ℓ – Species heat supply
- \tilde{e}^ℓ – Energy transfer
- M^ℓ – Species flux
- η^ℓ – Species entropy
- θ – Temperature

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

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

Constitutive relation for mechanics

$$\tilde{\rho}_0^c \hat{e}^c(\mathbf{F}^{e^c}, \rho_0^c)$$



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

- 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

$$\lambda_I^e = \sqrt{\mathbf{N}_I \cdot \mathbf{C}^e \mathbf{N}_I}$$

Possibilities for interconversion laws

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

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

- Strain Energy Dependencies –
Weighted by relative densities

$$\Pi^f = \frac{\rho^f}{\rho^f + \rho^c} \Pi^c$$

(Gurtin & Murdoch, 1975)

- Enzyme Kinetics – Introducing
additional species to the mixture

$$\Pi^f = \frac{\rho^f}{\rho^f + \rho^c + \rho^e} \Pi^c$$

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- Cell Signalling – Preferential growth in
damaged regions

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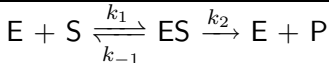
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$$\Pi^s = \frac{(\Pi_{max}^s \rho^s)}{(\rho_m^s + \rho^s)} \rho_{cell}, \quad \Pi^c = -\Pi^s$$

[Michaelis & Menten, 1913]

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Enzyme Kinetics

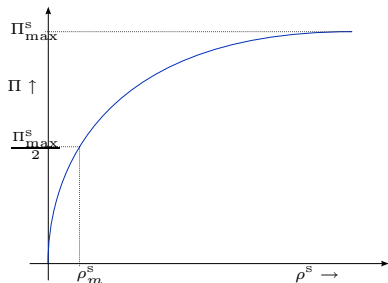


k_1 - Association of substrate and enzyme

k_{-1} - Dissociation of unaltered substrate

k_2 - Formation of product

$$\rho_m^s = \frac{(k_2 + k_{-1})}{k_1}$$



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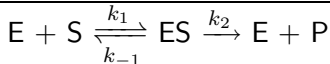
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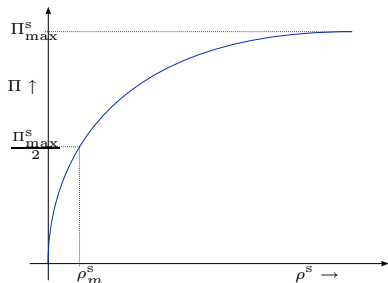


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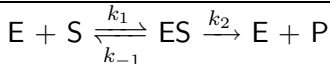
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