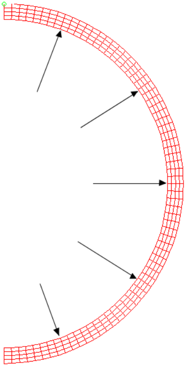
Growth and Remodeling
for Soft Tissue Deformation



Michelle Hine

Program in Applied Mathematics
Soft Tissue Biomechanics Laboratory
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October 25, 2013

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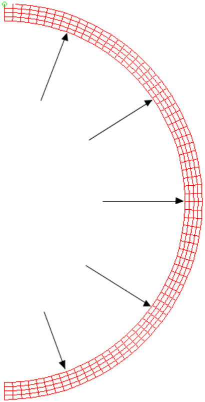

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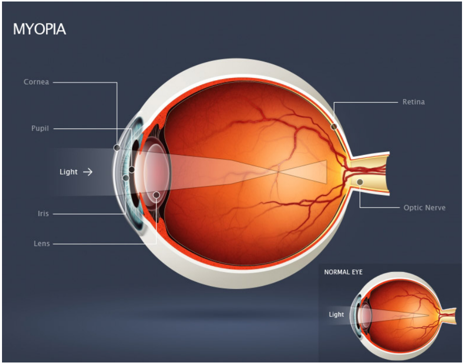
A Brief Overview of Myopia

- Distant images focus anterior to the retinal plane (nearsightedness)
- Affects 33.1% of Americans over the age of 20*
- Causes: Genetics, environmental factors
- Effects: Treatment complications, associated with glaucoma, retinal detachment

- Study this via growth law based on residual stresses



http://eyewiki.aao.org/Myopia

*Vitale S, Ellwein L, Cotch MF, Ferris FL, III, and Sperduto R. Prevalence of Refractive Error in the United States, 1999-2004. *Arch Ophthalmol.* 126, 2008, pp. 1111-1119.

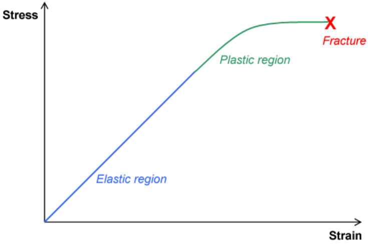
Table of Contents

Classical Mechanics

- Statistical mechanics
  - Follows individual particles (small length scale)
  - A HUGE number of items to track
  - Uses probability theory to relate the microscale to macroscopic properties of the system
- Continuum mechanics
  - Follows material at a continuum level (large length scale)
  - Locally averaged properties
  - Fundamental laws of physics—conservation of mass, momentum, energy

Preliminaries

- Elasticity
  - Reversible deformation
  - Ex. spring, rubber ball
  - Opposite of plasticity (ex. crumpled cars from a collision)



en.wikipedia.org/wiki/File:Stress-strain1.png

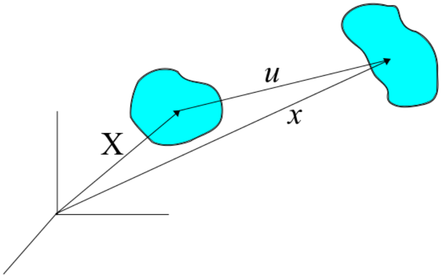
- Stress ("pressure")
  - Internal pressures that neighboring particles of a continuum exhibit upon one another
  - Dimension= $\frac{\text{force}}{\text{area}}$

$$\sigma = \frac{F}{A}$$

- Strain ("stretch")
  - Measurement of change in length relative to reference configuration length
  - Dimensionless

$$\varepsilon = \frac{\Delta L}{L}$$

Preliminaries

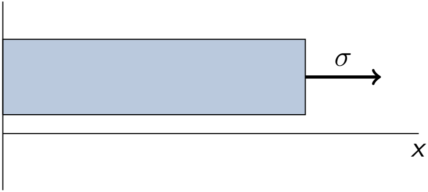


A point moves from undeformed configuration X to deformed configuration x over a period of time t

- Lagrangian formulation: $x(X, t)$ (follow the mass as it moves)
- Displacement: $u = x - X$

Motivational Example: Linear Elasticity

- Suppose we have a 1D linear elastic rod
- Pull on the rod with a constant tension
- What happens?
  Change in length is



$$F = \frac{\partial x}{\partial X}$$

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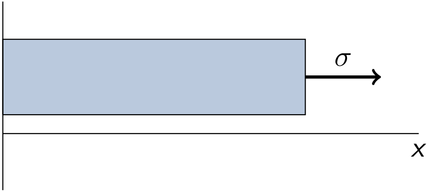
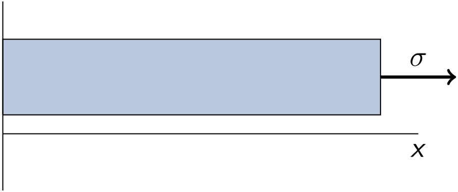
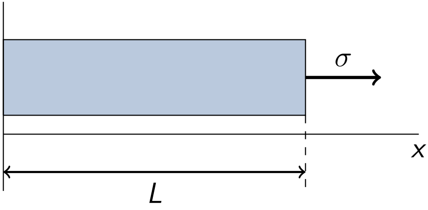




Motivational Example: Linear Elasticity

- Purely elastic $F = \dfrac{\partial x}{\partial X} = \alpha$
- Given linear elasticity,

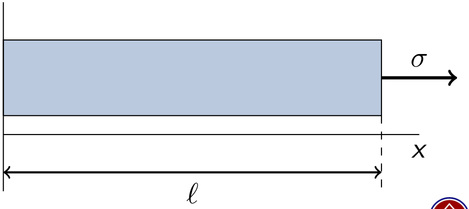
$$\sigma = E\epsilon = E(\alpha - 1)$$



- Stress $\sigma = 1.25\ Pa$, Young's modulus $E = 25\ Pa$

$$\Rightarrow \epsilon = 0.05, \alpha = 1.05$$

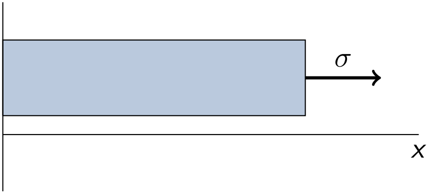
- $\ell = \alpha L$

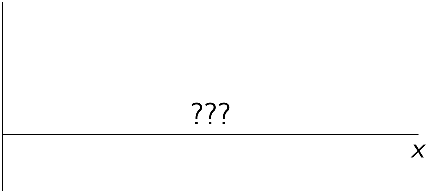


Example: Linear Elasticity & Growth

- What if we also want it to grow?
- Need: a growth law

$$\dot{\gamma} = \gamma(\alpha, \sigma, t)$$





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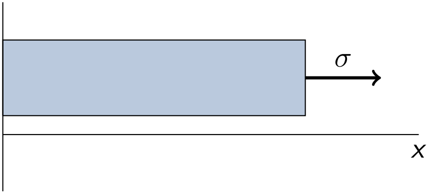
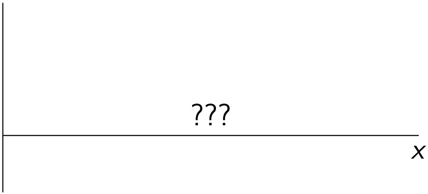


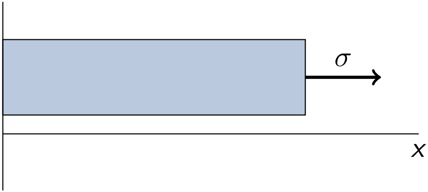
- Where does a growth law come from?
  - Experiments
  - It depends what is being modeled



Example: Linear Elasticity & Growth

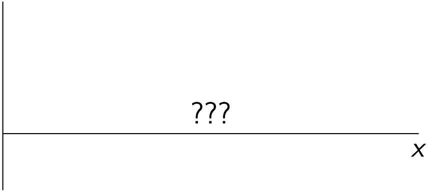
- Suppose

$$\begin{cases} \sigma = E(\alpha - 1) \\ \dot{\gamma} = k\gamma(\alpha - 1) \end{cases}$$



- Now two things are happening: elastic change and growth.
- Need an initial condition, so assume initially no growth

$$\gamma(0) = 1$$



Example: Linear Elasticity & Growth

- Suppose

$$\begin{cases} \sigma = E(\alpha - 1) \\ \dot{\gamma} = k\gamma(\alpha - 1) \\ \gamma(0) = 1 \end{cases}$$

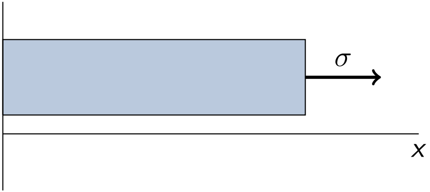
- $\sigma = 1.25\ Pa$, $E = 25\ Pa$

$$\Rightarrow \alpha = 1.05$$

- Then solve for growth

$$\gamma(t) = e^{k(\alpha-1)t}$$

$$\Rightarrow \gamma(t) = e^{0.05kt}$$



Example: Linear Elasticity & Growth

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- Then solve for growth

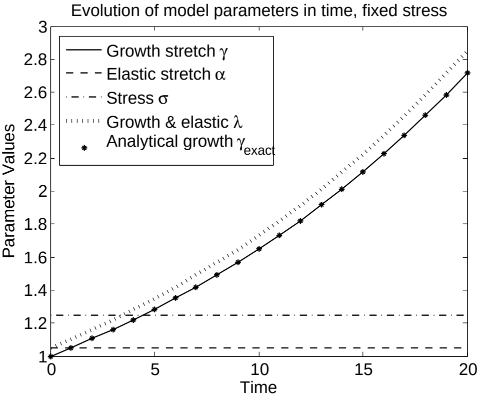
$$\gamma(t) = e^{k(\alpha-1)t}$$

$$\Rightarrow \gamma(t) = e^{0.05kt}$$

- Total deformation?

$$F = \alpha\gamma$$

- $\ell = \alpha\gamma L$



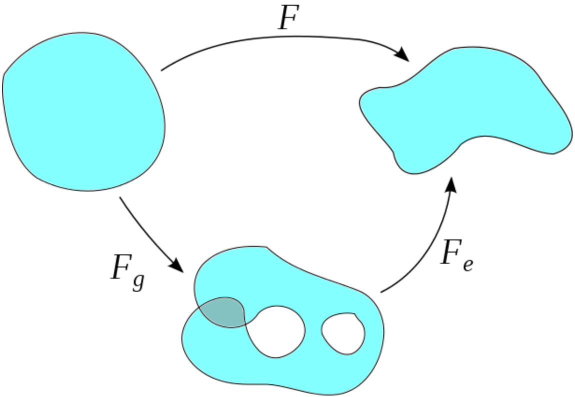
$k = 1$

Big Idea: Multiplicative Decomposition

- Idea: borrowed from plasticity

$$F = F_e F_g = \alpha\gamma$$

- Separation of time scales
  - Elastic—instantaneous vs. growth—days to months



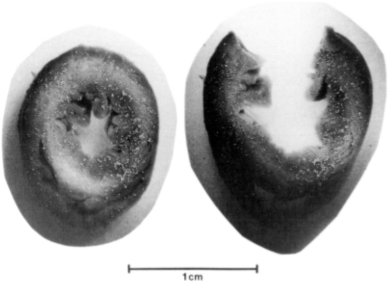
A Brief History of Growth

- 1968, Lee introduced a multiplicative split for elastoplasticity

$$\mathbf{F} = \mathbf{F}_e \mathbf{F}_p.$$

- 1981, Skalak adapted principles of finite elasticity to growth; incompatible growth fields result in residual stresses

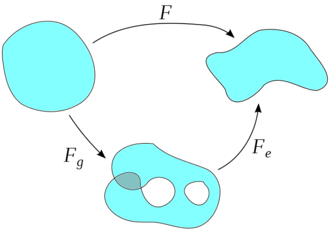
- 1990, Omens & Fung show hearts, arteries are under residual stress



Omens and Fung, 1990

Growth Incompatibility

- Growth deformation gradient $\mathbf{F}_g$ may cause growth
  - Fictitious intermediate configuration
  - Stress free state
  - $\mathbf{F}_g$ carried as an internal variable
- Elastic deformation gradient $\mathbf{F}_e$ enforces continuity
  - May build up residual stresses



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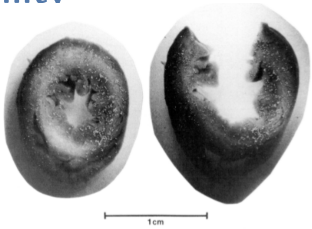
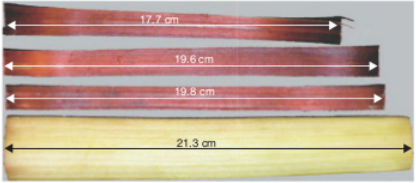
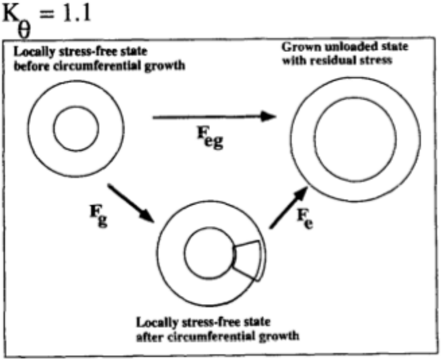




Omens & Fung, 1990; http://thechronicleflask.files.wordpress.com/; Vandiver & Goriely, 2008

Growth Incompatibility

- F_g is local stress-free state (fictitious)
- Residual stresses buildup may occur
  - Local incompatibility, e.g. cell grows independently of neighbors
  - Global incompatibility, e.g. smooth growth field that is not compatible (ring growth)
- Physically, only the original and grown, deformed states exist

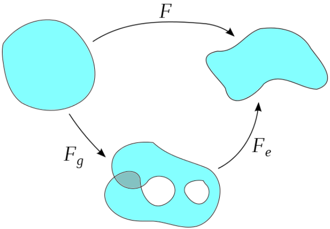


Rodriguez, Hoger, McCulloch, 1994

Growth vs. Remodeling

What does $\mathbf{F}_g$ do to the material?

- Growth
  - Change in volume
  - Material properties remain the same (e.g., density is preserved)
- Remodeling
  - Change in density
  - Volume remains the same
- Growth & Remodeling
  - Volume and density may change



Note: the final density and/or volume may change due to $\mathbf{F}_e$

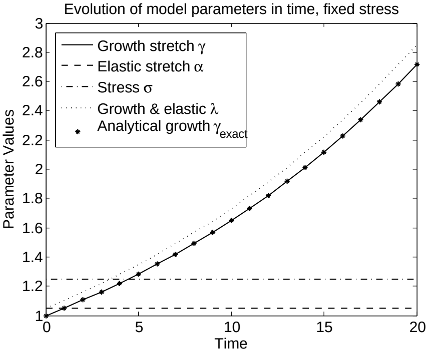
Growth Law

- Constitutive law
  - Formulated as a rate
  - Initial condition is always no growth

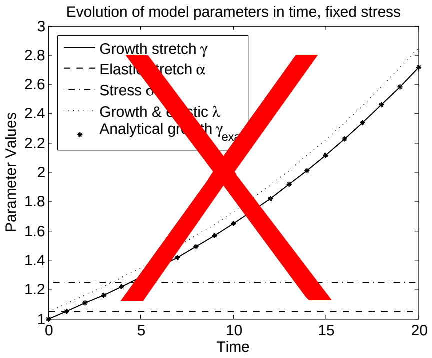
$$\gamma(0) = 1; \qquad \mathbf{F}_g(0) = \mathbf{I}$$

- What should growth depend on? What are we modeling?
  - Usually dependent on stress or strain
  - Cancer cells (e.g. original location)
  - Nutrient flow (e.g current location)
  - Additional growth sites (e.g. amount of growth)

Unlimited Growth



Unlimited Growth



- Biologically, this is bad.

Preventing Unlimited Growth

- Homeostatic stress/strain?

$$\dot{\vartheta}^g = f(\boldsymbol{\sigma} - \boldsymbol{\sigma}^*) \qquad \text{or} \qquad \dot{\vartheta}^g = h(\boldsymbol{\alpha} - \boldsymbol{\alpha}^*),$$

- Limited growth potential?

$$\dot{\vartheta}^g = k^g(\vartheta^g) f(\boldsymbol{\sigma}) \qquad \text{or} \qquad \dot{\vartheta}^g = k^g(\vartheta^g) h(\boldsymbol{\alpha})$$

Growth in Soft Tissues

- Himpel and Kuhl use $\mathrm{tr}(\mathbf{M^e})$, the trace of the Mandel stress

$$\mathbf{M^e} = \mathbf{C}_e \mathbf{S}_e,$$

where $\mathbf{C}_e = (\mathbf{F}_e)^T \mathbf{F}_e$; $\quad \mathbf{S}_e = f(\psi, \mathbf{C}_e)$; $\quad \psi$ is some energy

- Isotropic growth law

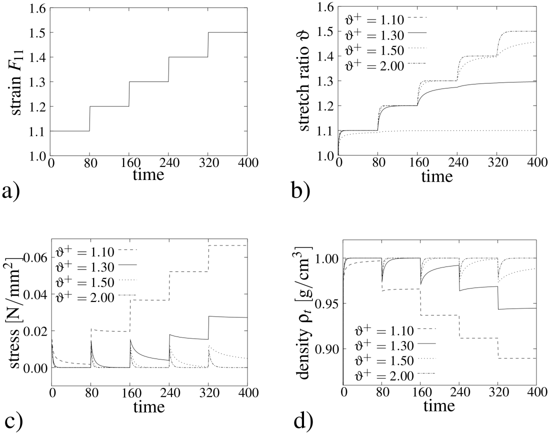
$$F_g = \vartheta \mathbf{I}, \qquad \dot{\vartheta}^g = k^g(\vartheta^g)\mathrm{tr}(\mathbf{M^e}),$$

$$k_\vartheta(\vartheta) = \begin{cases} k^+ \left(\dfrac{\vartheta^+ - \vartheta}{\vartheta^+ - 1}\right)^{m_\vartheta^+}, & \text{for } \mathrm{tr}(\mathbf{M^e}) > 0 \\ k^- \left(\dfrac{\vartheta - \vartheta^-}{1 - \vartheta^-}\right)^{m_\vartheta^-}, & \text{for } \mathrm{tr}(\mathbf{M^e}) < 0 \end{cases}.$$

- Mandel stress is energy conjugate to growth velocity gradient $\mathbf{L}_g$, which is used in an energy equation to derive stress-strain relationship

Limiting Growth: Effect of ϑ^+, ϑ^-

$$\dot{\vartheta}^g = k^g(\vartheta^g)\phi^g(\mathbf{M}^e), \qquad k^+\left(\frac{\vartheta^+ - \vartheta}{\vartheta^+ - 1}\right)^{m_\vartheta^+} \text{ for } \mathrm{tr}(\mathbf{M}^e) > 0$$



Himpel, et al. 2005

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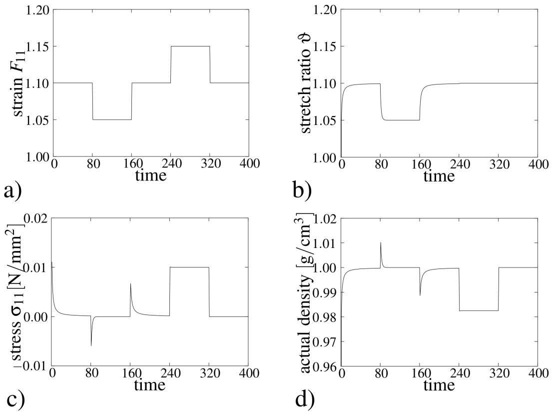
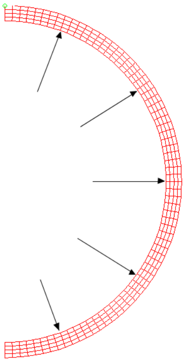


Himpel, et al. 2005

Model Description

- Computational domain is sclera (white part of the human eye), which moves
- Assumptions
  - Finite elasticity
  - Hyperelastic model, given energy function ψ
  - Quasi-steady state (inertial terms are negligible)
- Finite Element method
- Newton-Raphson iterations

- Axisymmetric formulation



General Equations of Elasticity

$\mathbf{x}$	deformed configuration	$\mathbf{f}$	body forces
$\mathbf{X}$	undeformed configuration	$\mathbf{C}$	right C-G strain, $\mathbf{F}^T\mathbf{F}$
$\mathbf{S}$	2nd Piola-Kirchhoff stress	ψ	strain energy density
$\mathbf{F}$	deformation gradient, $\frac{\partial \mathbf{x}}{\partial \mathbf{X}}$	P	pressure

- Lagrangian formulation; for $\hat{e}^i$ standard basis, $\nabla_0 \doteq \hat{e}^i \dfrac{\partial}{\partial X_i}$
- Quasistatic conservation of momentum, no body forces

$$\nabla_0 \cdot (\mathbf{F} \cdot \mathbf{S}) + \not{\mathbf{f}} = \mathbf{0}$$

- Hyperelastic stress-strain relationship

$$\mathbf{S} = \frac{\partial \psi}{\partial \mathbf{C}} = \frac{1}{2}\frac{\partial \psi}{\partial \mathbf{F}}$$

- Boundary conditions, e.g. $(\mathbf{F} \cdot \mathbf{S}) \cdot \mathbf{n} = -P \cdot \mathbf{n}$

General Equations of Growth

$\mathbf{F}$	deformation gradient	ϑ	isotropic growth stretch
$\mathbf{F_e}$	elastic tensor	$\mathbf{M^e}$	Mandel stress, $\mathbf{C_e} \cdot \mathbf{S_e}$
$\mathbf{F_g}$	growth tensor		

- Multiplicative decomposition

$$\mathbf{F} = \mathbf{F}_e \cdot \mathbf{F}_g$$

- Isotropic growth

$$\mathbf{F}_g = \vartheta \mathbf{I}$$

- Growth law

$$\dot{\vartheta} = k(\vartheta) \cdot \mathrm{tr}(\mathbf{M^e})$$

- Conservation of mass with source $\mathcal{R}_0$

$$\rho_0 = \rho_0^* + \int_{t_0}^{t} \mathcal{R}_0 d\bar{t}, \qquad \dot{\rho}_0 = \mathcal{R}_0$$

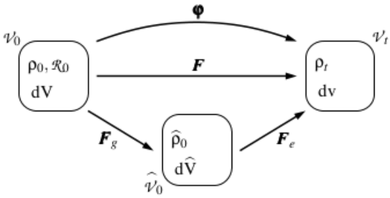
General Equations of Growth

- Isotropic growth

$$\mathbf{F}_g = \vartheta \mathbf{I}$$

- Then the growth Jacobian

$$J_g = \frac{d\widehat{V}}{dV} = \det(\mathbf{F}_g) = \vartheta^3$$



Himpel, et al. 2005

- With constant growth density $\widehat{\rho}_0 = \rho_0^*$

$$\rho_0 = J_g \widehat{\rho}_0 = \vartheta^3 \rho_0^*, \qquad \mathcal{R}_0 = \dot{\rho}_0 = 3\vartheta^2 \dot{\vartheta} \rho_0^*$$

ρ_0 density of the grown mass in the material configuration
ρ_0^* original density

Solving Growth Computationally

- For stability, update with backward Euler

$$\dot{\vartheta} = \frac{\vartheta - \vartheta^k}{\Delta t}$$

- Growth evolution is nonlinear, so Newton-Raphson iteration:

  Writing residual the $R_\vartheta = -\vartheta + \vartheta_n + \dot{\vartheta}\Delta t = 0$, the update growth multiplier is

$$\vartheta^{k+1} = \vartheta^k - K^{-1} R_\vartheta^k, \qquad \text{for } K = \frac{\partial R_\vartheta}{\partial \vartheta}$$

Solving Growth Computationally

$$\mathbf{F} = \mathbf{F}_e \cdot \mathbf{F}_g$$

- For each growth step, we know the total deformation of the step before (from FEM), so $\mathbf{F}$ is known; stress $\mathbf{M^e}$ is known
- Isotropic growth tensor may be calculated

$$\dot{\vartheta} = k(\vartheta) \cdot \mathrm{tr}(\mathbf{M^e}), \qquad \mathbf{F}_g = \vartheta \mathbf{I}$$

- The elastic deformation is

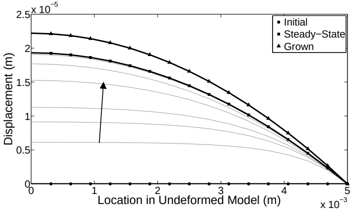
$$\mathbf{F}_e = \mathbf{F} \cdot \mathbf{F}_g^{-1}, \qquad \text{where } \mathbf{F}_g^{-1} = \frac{1}{\vartheta}\mathbf{I}$$

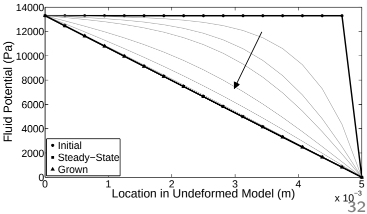
- Use $\mathbf{F}_e, \mathbf{F}_g$ to solve conservation of linear momentum
- Repeat

Previous Work

One-dimensional MPHETS with growth [Harper, 2012]

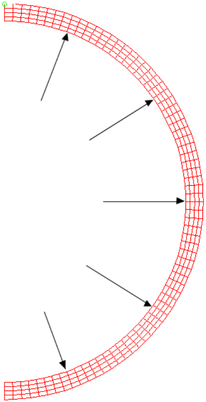
- Mixed Poro- variables u, p^f
  - Effective stress principle $S = S^{eff} - JHp^f$
  - Darcy's Law for fluid $\frac{\partial v_i^{fr}}{\partial x_i} + D_{kk} = 0$
- Hyperelastic $S_{ij} = \frac{\partial U}{\partial E_{ij}}$
- Mass Transport
  - Concentration $c = m^c / V^f$
  - Species flux $j_i^{cr} = cn(v_i^c - v_i^s)$
- Swelling fluid pressure + osmosis $p^f + p^o$
- Growth



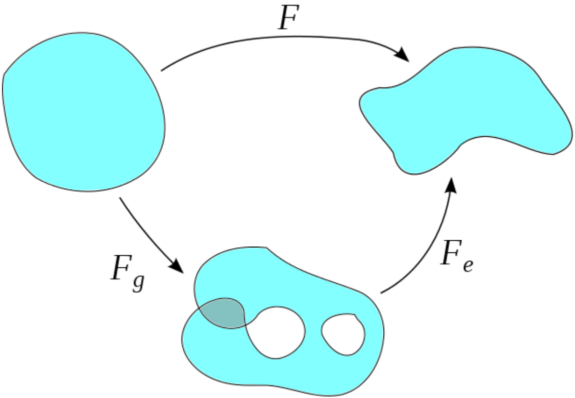


Future Work

- Code up hyperelastic growth model with finite strain
- Add poroelasticity
- Add constituent transport
- Osmosis?
- Model myopia? Other tissues?



Summary



Thank You!

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