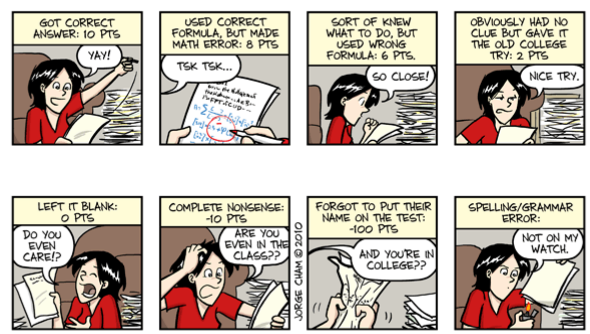
16 - everything grows!
midterm summary

day	date		topic
tue	jan	07	motivation - everything grows!
thu	jan	09	basics maths - notation and tensors
tue	jan	14	project example - growing skin
thu	jan	16	kinematics - growing brains
tue	jan	21	basic kinematics - large deformation and growth
thu	jan	23	kinematics - growing hearts
tue	jan	28	kinematics - growing leaflets
thu	jan	30	basic balance equations - closed and open systems
tue	feb	04	basic constitutive equations - growing muscle
thu	feb	06	basic constitutive equations - growing tumors
tue	feb	11	volume growth - finite elements for growth - theory
thu	feb	13	volume growth - finite elements for growth - matlab
tue	feb	18	basic constitutive equations - growing bones
thu	feb	20	density growth - finite elements for growth
tue	feb	25	density growth - growing bones
thu	feb	27	everything grows! - midterm summary
tue	mar	04	midterm
thu	mar	06	remodeling - remodeling arteries and tendons
tue	mar	11	class project - discussion, presentation, evaluation
thu	mar	13	class project - discussion, presentation, evaluation
thu	mar	14	written part of final projects due

me337 - goals

in contrast to traditional engineering structures living structures show the fascinating ability to **grow and adapt their form, shape and microstructure** to a given mechanical environment. this course addresses the phenomenon of growth on a theoretical and computational level and applies the resulting theories to classical biomechanical problems like bone remodeling, hip replacement, wound healing, atherosclerosis or in stent restenosis. this course will illustrate how classical engineering concepts like continuum mechanics, thermodynamics or finite element modeling have to be rephrased in the context of growth. having attended this course, you will be able to develop your own problemspecific finite element based numerical solution techniques and interpret the results of biomechanical simulations with the ultimate goal of improving your **understanding of the complex interplay between form and function**.

me 337 - grading



- 30 % homework - 3 homework assignments, 10% each
- 30 % midterm - closed book, closed notes, one single page cheat sheet
- 20 % final project oral presentations - graded by the class
- 20 % final project essay - graded by instructor

growth = change in mass

growth [ɡroʊθ] which is defined as **added mass**, can occur through

- hyperplasia / cell division
- hypertrophy / cell enlargement
- secretion of extracellular matrix
- accretion @external or internal surfaces

mass = volume x density

$$\frac{\textbf{mass}}{\textbf{changes}} = \frac{\textbf{volume}}{\textbf{changes}} \times \frac{\textbf{density}}{\textbf{changes}}$$

taber 'biomechanics of growth, remodeling and morphogenesis' [1995]

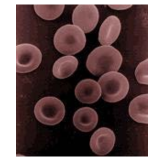
continuum mechanics

continuum hypothesis [kən'tɪn.ju.əm haɪ'pɑːθ.ə.sɪs]
we assume that the characteristic length scale of the microstructure is much smaller than the characteristic length scale of the overall problem, such that the properties at each point can be understood as averages over a characteristic length scale

$$l^{\text{micro}} \ll l^{\text{averg}} \ll l^{\text{conti}}$$

example: biomechanics

$$l^{\text{micro}} = l^{\text{cells}} \approx 10\mu\text{m}$$
$$l^{\text{conti}} = l^{\text{tissue}} \approx 10\text{cm}$$



continuum hypothesis can be applied to analyzing tissues

the continuum  equations

- kinematic equations – what's strain? $\epsilon = \frac{\Delta l}{l}$
  general equations that characterize the deformation of a physical body without studying its physical cause
- balance equations – what's stress? $\sigma = \frac{F}{A}$
  general equations that characterize the cause of motion of any body
- constitutive equations - how are they related? $\sigma = E\,\epsilon$
  material specific equations that complement the set of governing equations

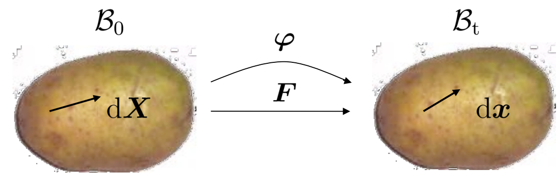
the continuum  equations

- kinematic equations - why not $\epsilon = \frac{\Delta l}{l}$?
  inhomogeneous deformation » non-constant
  finite deformation » non-linear $\boldsymbol{F} = \nabla_X \boldsymbol{\varphi}$
  inelastic deformation » growth tensor $\boldsymbol{F} = \boldsymbol{F}_{\text{e}} \cdot \boldsymbol{F}_{\text{g}}$
- balance equations - why not $\sigma = \frac{F}{A}$? $\text{Div}(\boldsymbol{P}) + \rho\, \boldsymbol{b}_0 = \boldsymbol{0}$
  equilibrium in deformed configuration » multiple stress measures
- constitutive equations - why not $\sigma = E\,\epsilon$?
  finite deformation » non-linear $\boldsymbol{P} = \boldsymbol{P}(\boldsymbol{F})$
  inelastic deformation » internal variables $\boldsymbol{P} = \boldsymbol{P}(\rho, \boldsymbol{F}, \boldsymbol{F}_{\text{g}})$

kinematic equations

kinematic equations [kɪnəˈmætɪk ɪˈkweɪ.ʒənz] describe the **motion of objects** without the consideration of the masses or forces that bring about the motion. the basis of kinematics is the choice of coordinates. the 1st and 2nd time derivatives of the position coordinates give the **velocities and accelerations.** the difference in placement between the beginning and the final state of two points in a body expresses the numerical value of **strain.** strain expresses itself as a change in size and/or shape.

kinematics equations



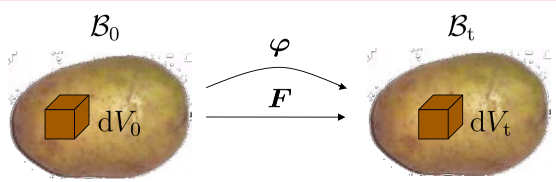
- transformation of line elements - deformation gradient F_{ij}

$$\mathrm{d}x_i = F_{ij}\,\mathrm{d}X_j \quad \text{with} \quad F_{ij} : T\mathcal{B}_0 \to T\mathcal{B}_t \qquad F_{ij} = \left.\frac{\partial \varphi_i}{\partial X_j}\right|_{t\ \text{fixed}}$$

- uniaxial tension (incompressible), simple shear, rotation

$$F_{ij}^{\mathrm{uni}} = \begin{bmatrix} \alpha & 0 & 0 \\ 0 & \alpha^{-\frac{1}{2}} & 0 \\ 0 & 0 & \alpha^{-\frac{1}{2}} \end{bmatrix} \quad F_{ij}^{\mathrm{shr}} = \begin{bmatrix} 1 & \gamma & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} \quad F_{ij}^{\mathrm{rot}} = \begin{bmatrix} \cos(\theta) & \sin(\theta) & 0 \\ -\sin(\theta) & \cos(\theta) & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

kinematic equations



- transformation of volume elements - determinant of $\boldsymbol{F}$

$$\mathrm{d}V_0 = \mathrm{d}\boldsymbol{X}_1 \cdot [\mathrm{d}\boldsymbol{X}_2 \times \mathrm{d}\boldsymbol{X}_3] \qquad \mathrm{d}V_t = \mathrm{d}\boldsymbol{x}_1 \cdot [\mathrm{d}\boldsymbol{x}_2 \times \mathrm{d}\boldsymbol{x}_3]$$
$$= \det([\mathrm{d}\boldsymbol{x}_1, \mathrm{d}\boldsymbol{x}_2, \mathrm{d}\boldsymbol{x}_3])$$
$$= \det([\mathrm{d}\boldsymbol{X}_1, \mathrm{d}\boldsymbol{X}_2, \mathrm{d}\boldsymbol{X}_3]) \qquad = \det(\boldsymbol{F})\,\det([\mathrm{d}\boldsymbol{X}_1, \mathrm{d}\boldsymbol{X}_2, \mathrm{d}\boldsymbol{X}_3])$$

- changes in volume - determinant of deformation gradient J

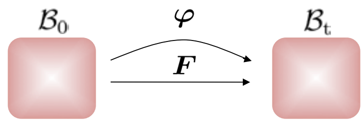
$$\mathrm{d}V_t = J\,\mathrm{d}V_0 \qquad J = \det(\boldsymbol{F})$$

volume growth

volume growth [ˈval.juːm ɡroʊθ] is conceptually comparable to thermal expansion. in linear elastic problems, growth stresses (such as thermal stresses) can be superposed on the mechanical stress field. in the nonlinear problems considered here, another approach must be used. the fundamental idea is to refer the strain measures in the constitutive equations of each material element to its current zero-stress configuration, which changes as the element grows.

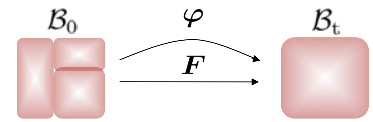
taber 'biomechanics of growth, remodeling and morphogenesis' [1995]

kinematics of finite growth



[1] consider an elastic body $\mathcal{B}_0$ at time t_0, unloaded & stressfree

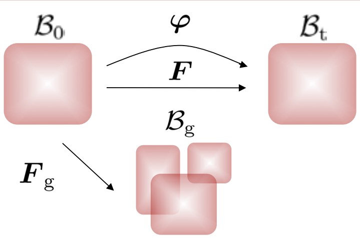
kinematics of finite growth



[1] consider an elastic body $\mathcal{B}_0$ at time t_0, unloaded & stressfree

[2] imagine the body is cut into infinitesimal elements each of which is allowed to undergo volumetric growth

kinematics of finite growth



[1] consider an elastic body $\mathcal{B}_0$ at time t_0, unloaded & stressfree

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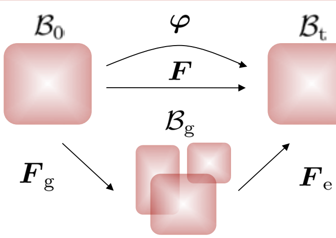
[3] after growing the elements, $\mathcal{B}_g$ may be incompatible

kinematics of finite growth



[1] consider an elastic body $\mathcal{B}_0$ at time t_0, unloaded & stressfree

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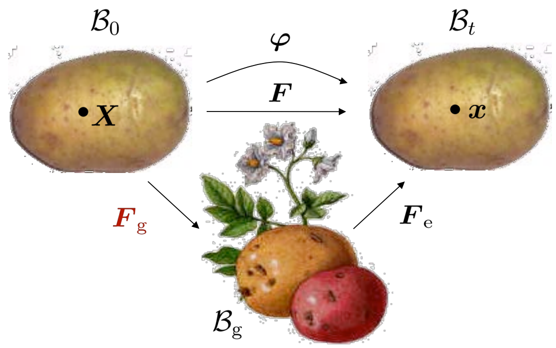
[4] loading generates compatible current configuration $\mathcal{B}_t$

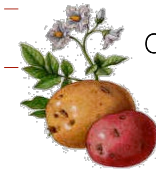
kinematics of finite growth



- incompatible growth configuration $\mathcal{B}_\mathrm{g}$ & growth tensor $\boldsymbol{F}_\mathrm{g}$

$$\boldsymbol{F} = \boldsymbol{F}_\mathrm{e} \cdot \boldsymbol{F}_\mathrm{g}$$

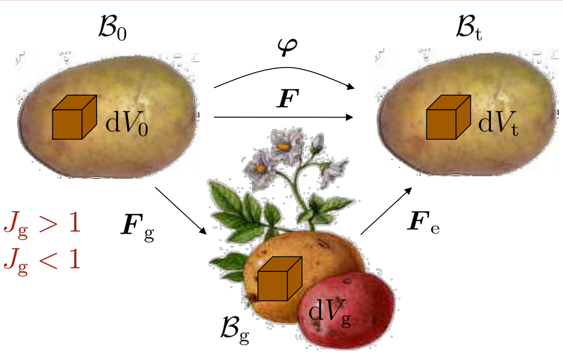
rodriguez, hoger & mc culloch [1994]



concept of incompatible growth configuration

biologically, the notion of **incompatibility** implies that subelements of the grown configuration may overlap or have gaps. the implication of incompatibility is the existence of residual stresses necessary to `squeeze` these grown subelements back together. mathematically, the notion of **incompatibility** implies that unlike the deformation gradient, $\boldsymbol{F} = \left.\frac{\partial \varphi}{\partial \boldsymbol{X}}\right|_{t \text{ fixed}}$ the growth tensor cannot be derived as a gradient of a vector field. incompatible configurations are useful in finite strain inelasticity such as viscoelasticity, thermoelasticity, elastoplasticity and growth.

kinematics of finite growth



growth $J_\mathrm{g} > 1$
resorption $J_\mathrm{g} < 1$

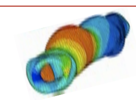
- changes in volume - determinant of growth tensor J_g

$$\mathrm{d}V_\mathrm{g} = J_\mathrm{g}\, \mathrm{d}V_0 \qquad J_\mathrm{g} = \det(\boldsymbol{F}_\mathrm{g})$$

kinematics – how does it grow?

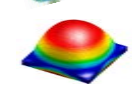
- isotropic volume growth

$$\boldsymbol{F}^\mathrm{g} = \vartheta\, \boldsymbol{I}$$



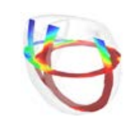
- transversely isotropic area growth

$$\boldsymbol{F}^\mathrm{g} = \sqrt{\vartheta}\, \boldsymbol{I} + [1 - \sqrt{\vartheta}]\, \boldsymbol{n}_0 \otimes \boldsymbol{n}_0$$



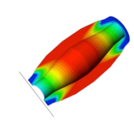
- transversely isotropic fiber growth

$$\boldsymbol{F}^\mathrm{g} = \boldsymbol{I} + [\vartheta - 1]\, \boldsymbol{f}_0 \otimes \boldsymbol{f}_0$$



- and various combinations thereof

$$\boldsymbol{F}^\mathrm{g} = \vartheta^\perp \boldsymbol{I} + [\vartheta^{||} - \vartheta^\perp]\, \boldsymbol{n}_0 \otimes \boldsymbol{n}_0$$



rodriguez, hoger, mc culloch [1994], taber [1995], epstein, maugin [2000], ambrosi, mollica [2002], goriely, ben amar [2007], kuhl, maas, himpel, menzel [2007], socci, rennati, gervaso, vena [2007], garikipati [2009], kroon, delhaas, arts, bovendeerd[2009], goktepe, abilez, kuhl[2010], böl, albero[2014]

kinetics – why does it grow?

- biochemically driven

$$\dot{\vartheta}^{\mathrm{g}} = k^{\mathrm{g}}(\vartheta^{\mathrm{g}})$$

- stress driven

$$\dot{\vartheta}^{\mathrm{g}} = k^{\mathrm{g}}(\vartheta^{\mathrm{g}})\,\phi^{\mathrm{g}}(\boldsymbol{M}^{\mathrm{e}})$$

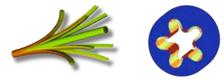
$$\phi^{\mathrm{g}} = \langle\, \mathrm{tr}(\boldsymbol{M}^{\mathrm{e}}) - p^{\mathrm{crit}} \rangle$$

- strain driven

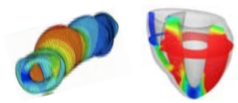
$$\dot{\vartheta}^{\mathrm{g}} = k^{\mathrm{g}}(\vartheta^{\mathrm{g}})\,\phi^{\mathrm{g}}(\boldsymbol{F}^{\mathrm{e}})$$

$$\phi^{\mathrm{g}} = \langle\, \vartheta^{\mathrm{e}}(\boldsymbol{F}^{\mathrm{e}}) - \vartheta^{\mathrm{crit}} \rangle$$

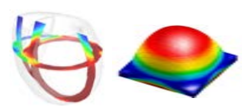
evolution



hypertension



hyperstretch



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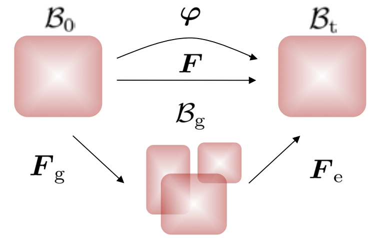
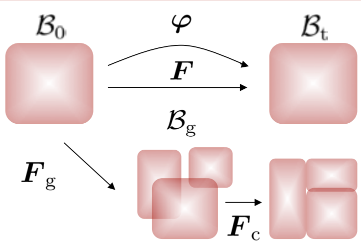
kinematics of finite growth



[3] after growing the elements, $\mathcal{B}_{\mathrm{g}}$ may be incompatible

[4] loading generates compatible current configuration $\mathcal{B}_{\mathrm{t}}$

kinematics of finite growth

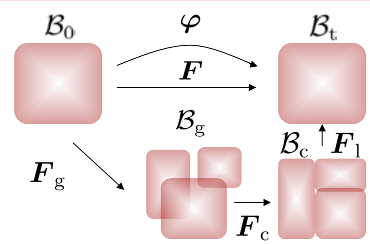


[3] after growing the elements, $\mathcal{B}_{\mathrm{g}}$ may be incompatible

[3a] we then first apply a deformation $\boldsymbol{F}_{\mathrm{c}}$ to squeeze the elements back together to the compatible configuration $\mathcal{B}_{\mathrm{c}}$

[4] to generate the compatible current configuration $\mathcal{B}_{\mathrm{t}}$

kinematics of finite growth



[3] after growing the elements, $\mathcal{B}_{\mathrm{g}}$ may be incompatible

[3a] we then first apply a deformation $\boldsymbol{F}_{\mathrm{c}}$ to squeeze the elements back together to the compatible configuration $\mathcal{B}_{\mathrm{c}}$

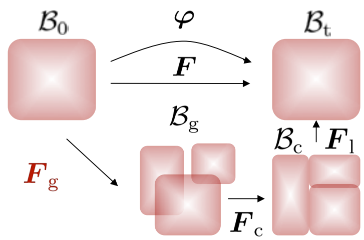
[3b] and then load the compatible configuration $\mathcal{B}_{\mathrm{c}}$ by $\boldsymbol{F}_{\mathrm{l}}$

[4] to generate the compatible current configuration $\mathcal{B}_{\mathrm{t}}$

kinematics of finite growth

$$\boldsymbol{F} = \boldsymbol{F}_{\mathrm{l}} \cdot \boldsymbol{F}_{\mathrm{c}} \cdot \boldsymbol{F}_{\mathrm{g}}$$

growth tensor $\boldsymbol{F}_{\mathrm{g}}$



$$\boldsymbol{F}_{\mathrm{e}} = \boldsymbol{F}_{\mathrm{l}} \cdot \boldsymbol{F}_{\mathrm{c}}$$

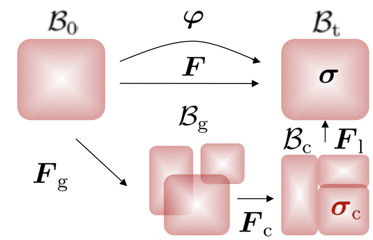
multiplicative decomposition

lee [1969], simo [1992], rodriguez, hoger & mc culloch [1994], epstein & maugin [2000], humphrey [2002], ambrosi & mollica [2002], himpel, kuhl, menzel & steinmann [2005]

kinematics of finite growth

$$\boldsymbol{F} = \boldsymbol{F}_{\mathrm{l}} \cdot \boldsymbol{F}_{\mathrm{c}} \cdot \boldsymbol{F}_{\mathrm{g}}$$

$\boldsymbol{F}_{\mathrm{g}}$



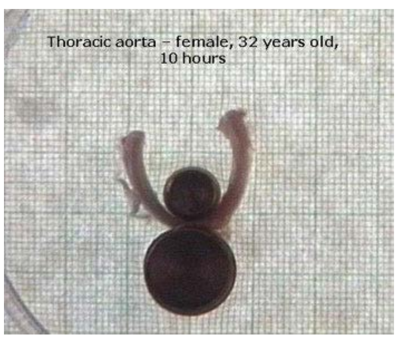
total stress

residual stress

residual stress

the additional deformation of squeezing the grown parts back to a compatible configuration gives rise to residual stresses (see thermal stresses)

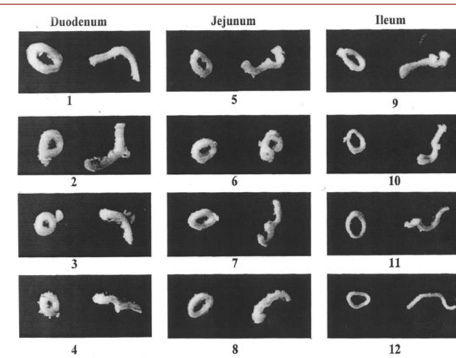
the classical opening angle experiment



an existence of residual strains in human arteries is well known. it can be observed as an opening up of a circular arterial segment after a radial cut. an opening angle of the arterial segment is used as a measure of the residual strains generally.

fung [1990], horný, chlup, zitný, mackov [2006]

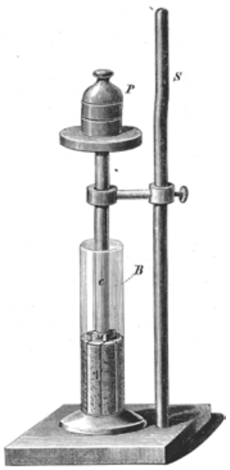
the classical opening angle experiment

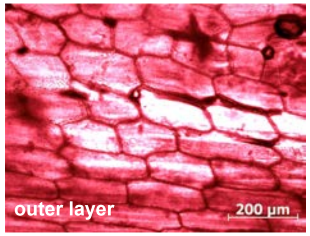


photographs showing specimens obtained from different locations in the intestine in the no-load state (left, closed rings) and the zero-stress state (right, open sectors). the rings of jejunum (site 5 to site 8) turned inside out when cut open

zhao, sha, zhuang, gregersen [2002]

residual stress in rhubarb



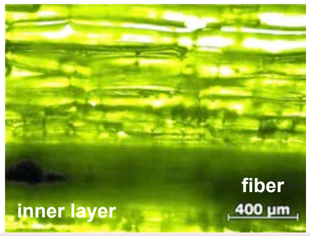


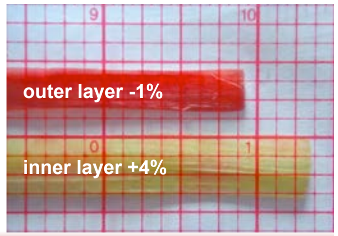
differential growth

outer layer
epidermis and collenchyma layers
tension - shortens by -1%

inner layer
parenchyma
compression - lengthens by +4%

residual stresses





müller [1880], vandiver, goriely [2009], kosmata, goriely, kuhl [2013]

concept of residual stress

constrained growth during development

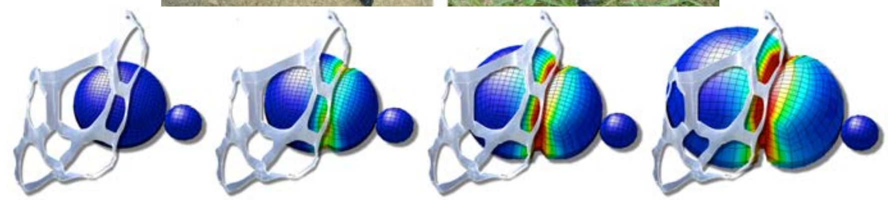
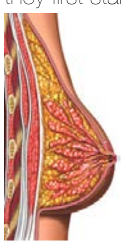


figure. growth-induced microenvironmental changes in a nine-year old female red-eared slider turtle trapped in a plastic six-pack ring. the turtle had worn the ring for five years. during this time, the ring had constrained the growth of the outer shell and created growth-induced stresses on the inner organs.

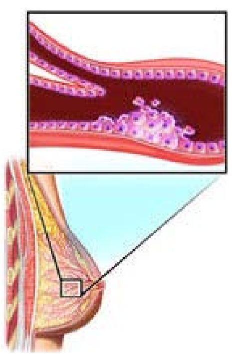
example - growing turtles

volume growth - cylindrical tumor

normal cells grow and multiply at a specific rate. cells that grow and multiply without stopping are called cancerous or malignant. however, they are not detectable when they first start growing.



invasive or infiltrating ductal carcinoma is the most common type of breast cancer. it occurs when the cells that line the milk duct become abnormal and spread into the surrounding breast tissue.



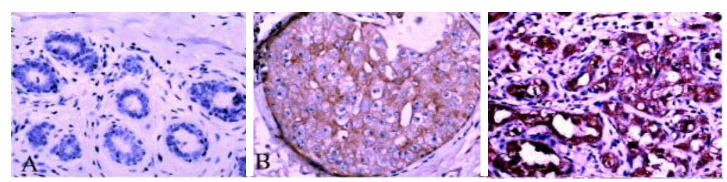
ductal carcinoma in situ is a non-invasive change in the cells that line the milk tubes that bring milk from the milk lobules to the nipple

example - breast cancer

volume growth - cylindrical tumor

model assumptions

- ductal cardinoma - tumor grows in breast duct for up to 10 cm
- model - homogeneous growth inside a rigid cylinder
- assumption - rotational symmetry
- strategy - solve for deformation that satisfies equi'm and boundary cond's



normal ductal epithelial cells (negative) | tumor cells of ductal carcinoma (positive) | invasive ductal carcinoma cells (strongly positive)

kinematic coupling of growth and deformation

example - breast cancer

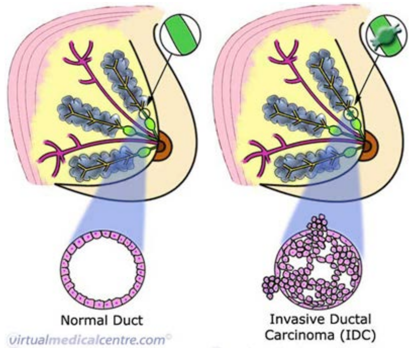
volume growth - cylindrical tumor

- homogeneous deformation inside a rigid cylinder

$$x = X \qquad y = Y \qquad z = \lambda Z$$

- deformation gradient

$$\boldsymbol{F} = \nabla_X \varphi \qquad \boldsymbol{F} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & \lambda \end{bmatrix}$$

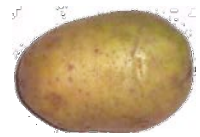


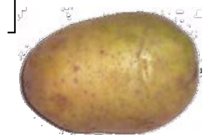
kinematic coupling of growth and deformation

volume growth - cylindrical tumor

$$\boldsymbol{F} = \nabla_X \varphi$$

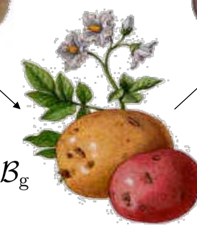
$$\mathcal{B}_0 \qquad \boldsymbol{F} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & \lambda \end{bmatrix} \qquad \mathcal{B}_t$$





$$\boldsymbol{F}_{\mathrm{g}} = \vartheta\, \boldsymbol{I} \qquad \boldsymbol{F}_{\mathrm{e}} = \boldsymbol{F} \cdot \boldsymbol{F}_{\mathrm{g}}^{-1}$$

$$\boldsymbol{F}_{\mathrm{g}} = \begin{bmatrix} \vartheta & 0 & 0 \\ 0 & \vartheta & 0 \\ 0 & 0 & \vartheta \end{bmatrix} \qquad \mathcal{B}_{\mathrm{g}} \qquad \boldsymbol{F}_{\mathrm{e}} = \begin{bmatrix} \frac{1}{\vartheta} & 0 & 0 \\ 0 & \frac{1}{\vartheta} & 0 \\ 0 & 0 & \frac{\lambda}{\vartheta} \end{bmatrix}$$



ambrosi & mollica [2002]

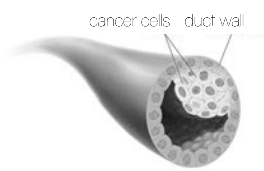
volume growth - cylindrical tumor

- stress

$$\boldsymbol{\sigma}_{\mathrm{e}} = \begin{bmatrix} \sigma_{xx} & 0 & 0 \\ 0 & \sigma_{yy} & 0 \\ 0 & 0 & \sigma_{zz} \end{bmatrix}$$

$$\sigma_{xx} = \sigma_{yy} = \mu \frac{\vartheta^3}{\lambda} \left[\frac{1}{\vartheta^2} - \left[\frac{\lambda}{\vartheta^3} \right]^q \right]$$

$$\sigma_{zz} = \mu \frac{\vartheta^3}{\lambda} \left[\frac{\lambda^2}{\vartheta^2} - \left[\frac{\lambda}{\vartheta^3} \right]^q \right]$$



- bc's $\quad \sigma_{zz} = 0$
- axial displacement λ as a function of growth ϑ

$$\lambda = \vartheta^{[2-3q]/[2-q]}$$

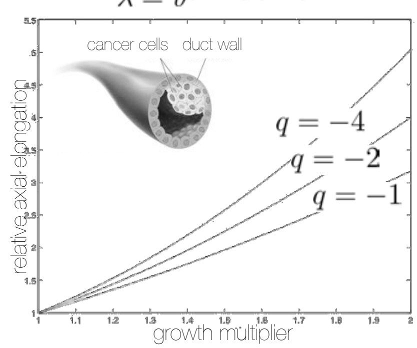
- growth induced stress σ_{xx} on tumor wall

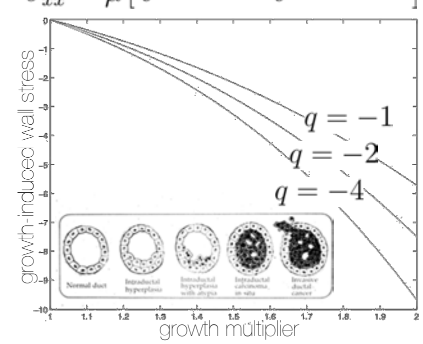
$$\sigma_{xx} = \mu \left[\vartheta^{2q/[2-q]} - \vartheta^{[4-4q]/[2-q]} \right]$$

ambrosi & mollica [2002]

volume growth - cylindrical tumor

$$\lambda = \vartheta^{[2-3q]/[2-q]} \qquad \sigma_{xx} = \mu \left[\vartheta^{2q/[2-q]} - \vartheta^{[4-4q]/[2-q]} \right]$$





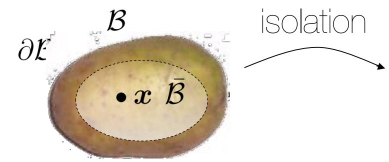
tumor pressure on duct walls increases with growth

ambrosi & mollica [2002]

balance equations

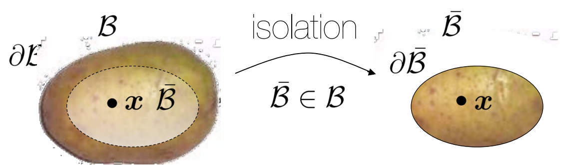
balance equations [ˈbæl.əns ɪˈkweɪ.ʒəns] of mass, momentum, angular momentum and energy, supplemented with an entropy inequality constitute the set of conservation laws. the law of **conservation of mass**/matter states that the **mass of a closed system** of substances will remain **constant**, regardless of the processes acting inside the system. the principle of conservation of momentum states that the total momentum of a closed system of objects is constant.

balance equations



[1] isolation of subset $\bar{\mathcal{B}}$ from $\mathcal{B}$

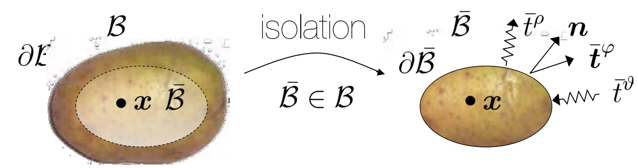
balance equations



[1] isolation of subset $\bar{\mathcal{B}}$ from $\mathcal{B}$

[2] characterization of influence of remaining body through phenomenological quantities - contact fluxes $\bar{t}^{\rho}$, $\bar{\boldsymbol{t}}^{\varphi}$ & $\bar{t}^{\vartheta}$

balance equations



[1] isolation of subset $\bar{\mathcal{B}}$ from $\mathcal{B}$

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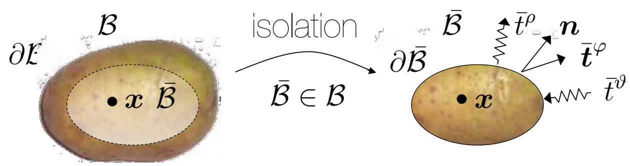
[3] definition of basic physical quantities - mass, linear and angular momentum, energy

balance equations



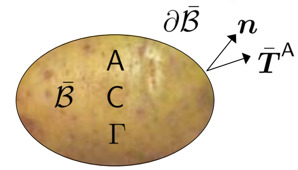
[1] isolation of subset $\bar{\mathcal{B}}$ from $\mathcal{B}$

[2] characterization of influence of remaining body through phenomenological quantities - contact fluxes $\bar{t}^{\rho}$, $\bar{\boldsymbol{t}}^{\varphi}$ & $\bar{t}^{\vartheta}$

[3] definition of basic physical quantities - mass, linear and angular momentum, energy

[4] postulation of balance of these quantities

generic balance equation - closed systems



general format

A ... balance quantity

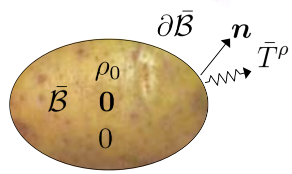
B ... flux $\quad \mathbf{B} \cdot \boldsymbol{n} = \bar{\boldsymbol{T}}^{\mathsf{A}}$

C ... source

Γ ... production

$$\mathrm{D}_t \mathsf{A} = \mathrm{Div}(\mathbf{B}) + \mathsf{C} + \Gamma$$

balance of mass - closed systems



balance of mass

ρ_0 ... density

$\mathbf{0}$ ... no mass flux $\quad \bar{T}^{\rho} = 0$

0 ... no mass source

0 ... no mass production

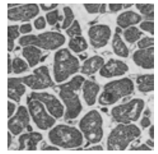
continuity equation $\quad \mathrm{D}_t \rho_0 = 0$

thermodynamic systems - open systems

open system [ˈoʊ.pən ˈsɪs.təm] thermodynamic system which is allowed to exchange mechanical work, heat and mass, typically $\boldsymbol{P} = \boldsymbol{P}(\nabla\varphi, ...)$, $\boldsymbol{Q} = \boldsymbol{Q}(\nabla\theta, ...)$ and $\boldsymbol{R} = \boldsymbol{R}(\nabla\rho, ...)$ with its environment. enclosed by a deformable, diathermal, permeable membrane. characterized through its state of deformation φ, temperature θ and density ρ.

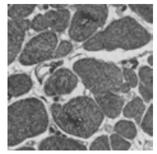
balance of mass - open systems

$$\mathrm{D}_t \rho_0 = \mathrm{Div}(\boldsymbol{R}) + \mathcal{R}_0$$



mass flux $\boldsymbol{R}$

- cell movement (migration)



mass source $\mathcal{R}_0$

- cell growth (proliferation)
- cell division (hyperplasia)
- cell enlargement (hypertrophy)

biological equilbrium

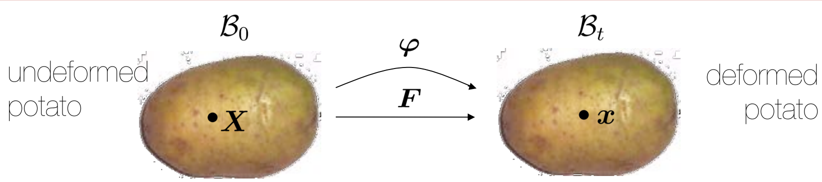
cowin & hegedus [1976], beaupré, orr & carter [1990], harrigan & hamilton [1992], jacobs, levenston, beaupré, simo & carter [1995], huiskes [2000], carter & beaupré [2001]

constitutive equations

constitutive equations [kənˈstɪ.tu.tɪv ɪˈkweɪ.ʒəns] in structural analysis, constitutive relations **connect applied stresses** or forces **to strains** or deformations. the constitutive relations for linear materials are linear. more generally, in physics, a constitutive equation is a relation between two physical quantities (often tensors) that is specific to a material, and does not follow directly from physical law. some constitutive equations are **simply phenomenological**; others are **derived from first principles**.

Wikipedia
The Free Encyclopedia

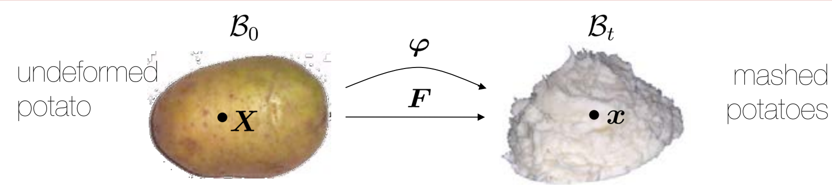
neo hooke'ian elasticity



- free energy $\psi_0^{\mathrm{neo}} = \frac{1}{2}\lambda_0 \ln^2(\det(\boldsymbol{F})) + \frac{1}{2}\mu_0[\,\boldsymbol{F}^{\mathrm{t}} \cdot \boldsymbol{F} : \boldsymbol{I} - n^{\mathrm{dim}} - 2\ln(\det(\boldsymbol{F}))\,]$
- definition of stress

$$\boldsymbol{P}^{\mathrm{neo}} = \mathrm{D}_{\boldsymbol{F}}\psi_0^{\mathrm{neo}} = \mu_0\,\boldsymbol{F} + [\,\lambda_0 \ln(\det(\boldsymbol{F})) - \mu_0\,]\,\boldsymbol{F}^{\text{-t}}$$

neo hooke'ian elasticity



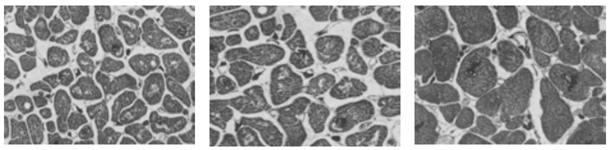
- free energy $\psi^{\mathrm{neo}} = \frac{1}{2}\lambda \ln^2(\det(\boldsymbol{F})) + \frac{1}{2}\mu[\,\boldsymbol{F}^{\mathrm{t}} \cdot \boldsymbol{F} : \boldsymbol{I} - n^{\mathrm{dim}} - 2\ln(\det(\boldsymbol{F}))\,]$
- definition of stress

$$\boldsymbol{P}^{\mathrm{neo}} = \rho_0 \mathrm{D}_{\boldsymbol{F}}\psi = \mu\,\boldsymbol{F} + [\,\lambda \ln(\det(\boldsymbol{F})) - \mu\,]\,\boldsymbol{F}^{\text{-t}}$$

- remember! mashing potatoes is not an elastic process!

volume growth at constant density

- free energy $\psi_0 = \psi_0^{\mathrm{neo}}(\boldsymbol{F}_{\mathrm{e}})$
- stress $\boldsymbol{P}_{\mathrm{e}} = \boldsymbol{P}_{\mathrm{e}}^{\mathrm{neo}}(\boldsymbol{F}_{\mathrm{e}})$
- growth tensor $\boldsymbol{F}_{\mathrm{g}} = \vartheta\,\boldsymbol{I}$ $\quad \mathrm{D}_t\vartheta = \underbrace{k_\vartheta(\vartheta)}_{\text{growth function}}\,\underbrace{\mathrm{tr}(\boldsymbol{C}_{\mathrm{e}}\cdot\boldsymbol{S}_{\mathrm{e}})}_{\text{pressure}}$
- mass source $\mathcal{R}_0 = 3\,\rho_0\vartheta^2\mathrm{D}_t\vartheta$ increase in mass

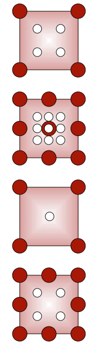


kinematic coupling of growth and deformation

rodriguez, hoger & mc culloch [1994], epstein & maugin [2000], humphrey [2002]

volume growth 49

integration point based solution of growth equation



- loop over all time steps
  - global newton iteration
    - loop over all elements
      - loop over all quadrature points
        - local newton iteration to determine ϑ_{n+1}
      - determine element residual & partial derivative
    - determine global residual and iterational matrix
  - determine φ_{n+1}
- determine state of biological equilibrium

growth multiplier ϑ as internal variable

volume growth - finite element method 50

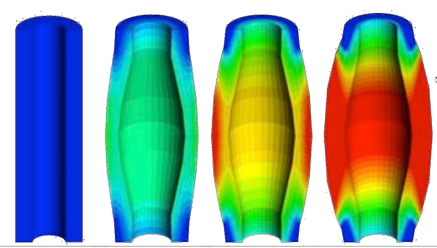
in-stent restenosis

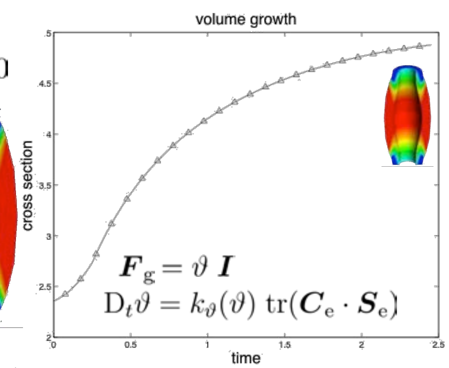
restenosis is the reoccurrence of stenosis, the narrowing of a blood vessel, leading to restricted blood flow. restenosis usually pertains to a blood vessel that has become narrowed, received treatment, and subsequently became renarrowed. in some cases, surgical procedures to widen blood vessels can cause further narrowing. during balloon angioplasty, the balloon 'smashes' the plaques against the arterial wall to widen the size of the lumen. however, this damages the wall which re-sponds by using physiological mechanisms to repair the damage and the wall thickens.

Wikipedia
The Free Encyclopedia

example - stenting and restenosis 51

qualitative simulation of stent implantation



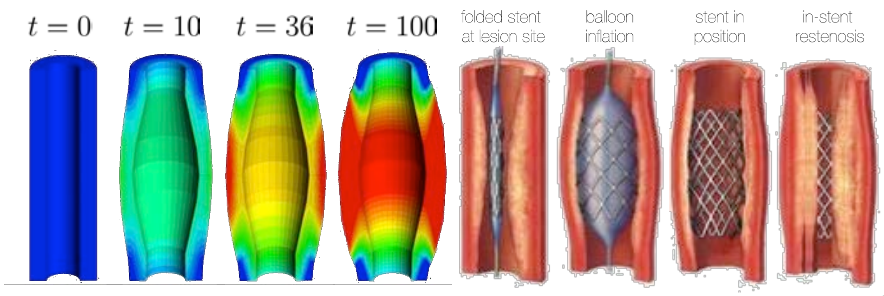


stress-induced volume growth

kuhl, maas, himpel & menzel [2007]

example - stenting and restenosis 52

qualitative simulation of stent implantation

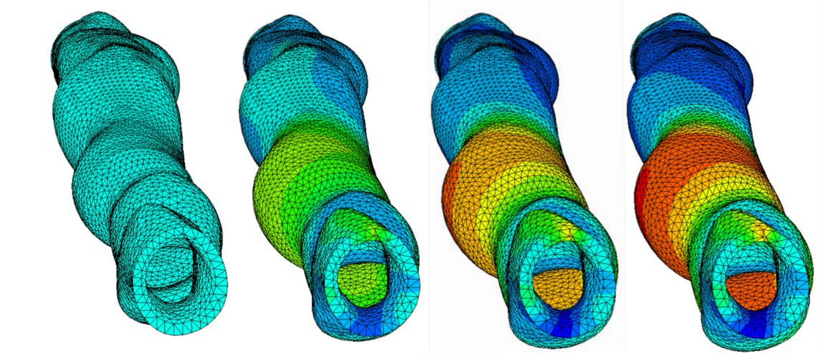


stress-induced volume growth

kuhl, maas, himpel & menzel [2007]

example - stenting and restenosis

virtual stent implantation - patient specific model



tissue growth - response to virtual stent implantation

kuhl, maas, himpel & menzel [2007]

example - stenting and restenosis

skin expansion

skin expansion is a technique used by plastic and restorative surgeons to cause the body grow additional skin. keeping living tissues under tension causes new cells to form and the amount of tissue to increase. in some cases, this may be accomplished by the implantation of inflatable balloons under the skin. by far the most common method, the surgeon inserts the inflatable expander beneath the skin and periodically, over weeks or months, injects a saline solution to slowly stretch the overlying skin. the growth of tissue is permanent, but will retract to some degree when the expander is removed. within the past 30 years, skin expansion has revolutionized recon-structive surgery. typical applications are breast reconstruction, burn injuries, and pediatric plastic surgery.

Wikipedia
The Free Encyclopedia

example - skin expansion

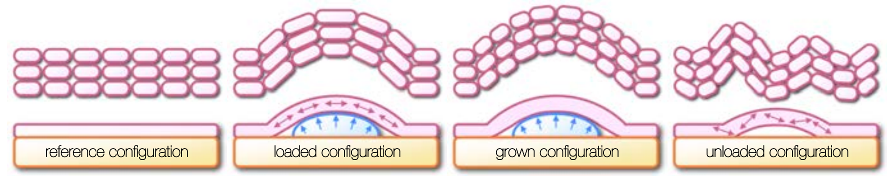
skin expansion and growth - facial reconstruction

in this study of reconstruction of the forehead in children, the average number of surgical procedures required to complete reconstruction was six, involving an average of three tissue expansion proecures.

gosain & cortes [2007]

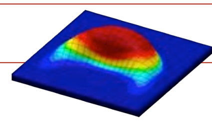
example - skin expansion

schematic sequence of tissue expansion



at biological equilibrium, the skin is in a physiological state of resting tension. a tissue expander is implanted subcutaneously between the skin and the hypodermis. when the expander is inflated, mechanical stretch induces cell proliferation causing the skin to grow. growth restores the state of resting tension. expander deflation reveals residual stresses in the skin layer.

volume growth at constant density



- deformation gradient

$$\boldsymbol{F} = \boldsymbol{F}^{\mathrm{e}} \cdot \boldsymbol{F}^{\mathrm{g}} \qquad \text{with} \qquad \boldsymbol{F} = \nabla_{\boldsymbol{X}} \varphi$$

- jacobians ... remember: volume change

$$J = J^{\mathrm{e}}\, J^{\mathrm{g}} \qquad \text{with} \qquad J = \det(\boldsymbol{F})$$

$$J^{\mathrm{e}} = \det(\boldsymbol{F}^{\mathrm{e}}) \text{ and } J^{\mathrm{g}} = \det(\boldsymbol{F}^{\mathrm{g}})$$

- area change

$$\vartheta = \vartheta^{\mathrm{e}}\, \vartheta^{\mathrm{g}} \qquad \text{with} \qquad \vartheta = ||\,\mathrm{cof}(\boldsymbol{F}) \cdot \boldsymbol{n}_0\,||$$

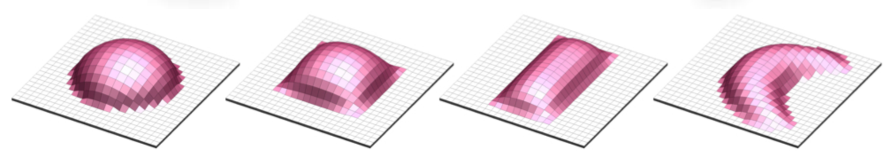
$$\vartheta^{\mathrm{e}} = ||\,\mathrm{cof}(\boldsymbol{F}^{\mathrm{e}}) \cdot \boldsymbol{n}_0\,|| \text{ and } \vartheta^{\mathrm{g}} = ||\,\mathrm{cof}(\boldsymbol{F}^{\mathrm{g}}) \cdot \boldsymbol{n}_0\,||$$

- growth tensor ... growth = area change

$$\boldsymbol{F}^{\mathrm{g}} = \sqrt{\vartheta^{\mathrm{g}}}\, \boldsymbol{I} + [\,1 - \sqrt{\vartheta^{\mathrm{g}}}\,]\; \boldsymbol{n}_0 \otimes \boldsymbol{n}_0$$

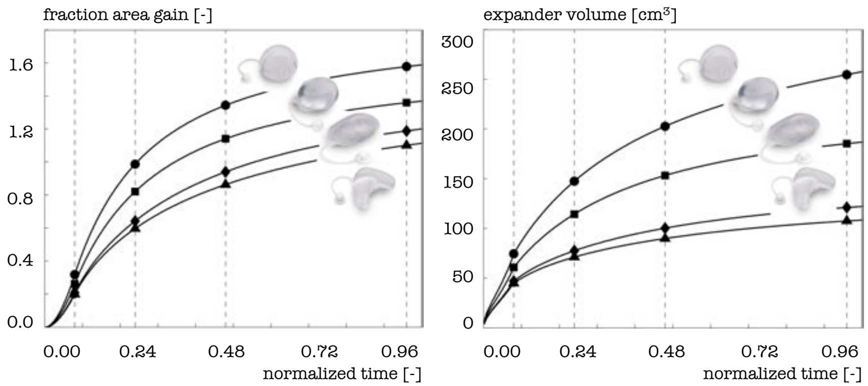
the adrian model [2010]

skin expander inflation and deflation



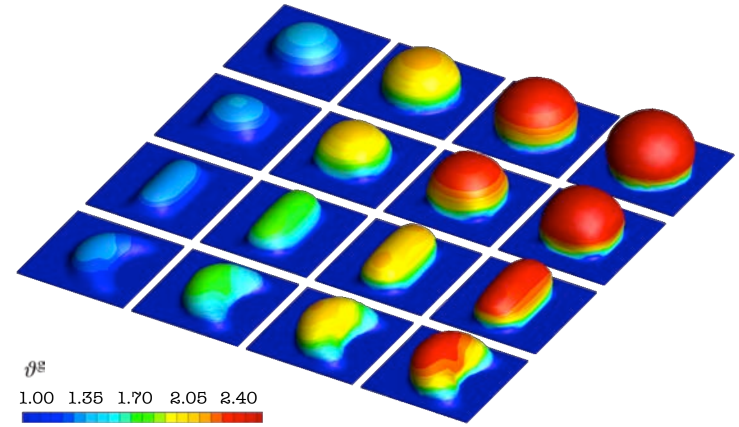
skin is modeled as a 0.2cm thin 12x12cm^2 square sheet, discretized with 3x24x24=1728 trilinear brick elements, with 4x25x25=2500 nodes and 7500 degrees of freedom. the base surface area of all expanders is scaled to 148 elements corresponding to 37cm^2. this area, shown in red, is gradually pressurized from below while the bottom nodes of all remaining elements, shown in white, are fixed.

area gain and expander volume



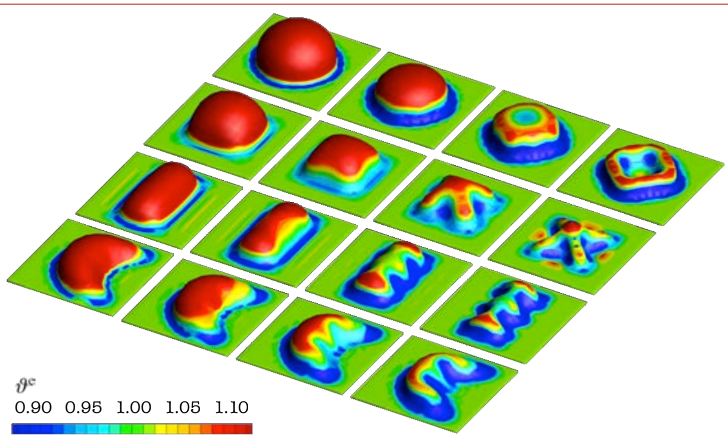
tissue expander inflation. expanders are inflated gradually between t=0.00 and t=0.08 by linearly increasing the pressure, which is then held constant from t=0.08 to t=1.00 to allow the skin to grow. under the same pressure, the circular expander displays the largest fractional area gain and expander volume, followed by the square, the rectangular, and the crescent-shaped expanders.

area growth – comparison of four expanders



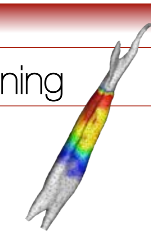
tissue expander inflation. spatio-temporal evolution of area growth. under the same pressure applied to the same base surface area, the circular expander induces the largest amount of growth followed by the square, the rectangular, and the crescent-shaped expanders.

elastic area stretch – comparison of four expanders



tissue expander deflation. spatio-temporal evolution of elastic area stretch. as the expander pressure is gradually removed, from left to right, the grown skin layer collapses. deviations from a flat surface after total unloading, right, demonstrate the irreversibility of the growth process.

stretch-induced muscle fiber lengthening



- deformation gradient

$$\boldsymbol{F} = \boldsymbol{F}^{e} \cdot \boldsymbol{F}^{g} \quad \text{with} \quad \boldsymbol{F} = \nabla_X \boldsymbol{\varphi}$$

- volume change

$$J = J^{e}\, J^{g} \quad \text{with} \quad J = \det(\boldsymbol{F}) > 0$$

- fiber stretch

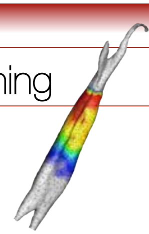
$$\lambda = \lambda^{e}\, \lambda^{g} \quad \text{with} \quad \lambda = [\, \boldsymbol{n}_0 \cdot \boldsymbol{F}^{t} \cdot \boldsymbol{F} \cdot \boldsymbol{n}_0 \,]^{1/2}$$

- growth tensor

$$\boldsymbol{F}^{g} = \boldsymbol{I} + [\, \vartheta - 1 \,]\, \boldsymbol{n}_0 \otimes \boldsymbol{n}_0 \qquad \vartheta = \lambda^{g}$$

zöllner, abilez, böl, kuhl [2012]

stretch-induced muscle fiber lengthening



- growth tensor

$$\boldsymbol{F}^{\mathrm{g}} = \boldsymbol{I} + [\,\vartheta - 1\,]\; \boldsymbol{n}_0 \otimes \boldsymbol{n}_0$$

- fiber lengthening

$$\dot{\vartheta} = k(\vartheta)\,\phi(\lambda^{\mathrm{e}})$$

- weighting function

$$k^{\mathrm{g}} = [[\vartheta^{\max} - \vartheta^{\mathrm{g}}]/[\vartheta^{\max} - 1]]^{\gamma}/\tau$$

- growth criterion

$$\phi = \langle \lambda^{\mathrm{e}} - \lambda^{\mathrm{crit}} \rangle = \langle \lambda\,/\,\vartheta - \lambda^{\mathrm{crit}} \rangle$$

zöllner, abilez, böl, kuhl [2012]

example 01 - limb lengthening

limb lengthening is a highly invasive surgical procedure to reconstruct or correct congenital and developmental deformities, post-traumatic injuries, regions of tumor removal, and **short statue**. using the principle of **distraction osteogenesis**, the surgeon cuts the bone in two and gradually pulls apart the two ends, triggering new bone to form. while the **main goal of osteodistraction is to lengthen the bone** itself, it is key to the procedure that the **surrounding muscle grows in parallel** with the stretched bone. contracture, the lack of appropriate muscle adaptation, is a

major source of complication during limb lengthening. optimal results can be obtained by lengthening the bone at a rate of **1mm per day, up to no more than 20%** of its initial length. although it is well accepted that mechanical factors play a limiting role in bone lengthening, to date, there are no mechanistic models that provide a scientific interpretation of these **empirical guidelines**.

limb lengthening experiment in rabbits

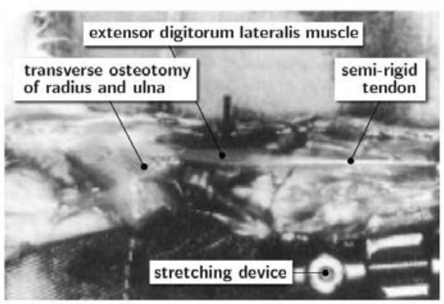
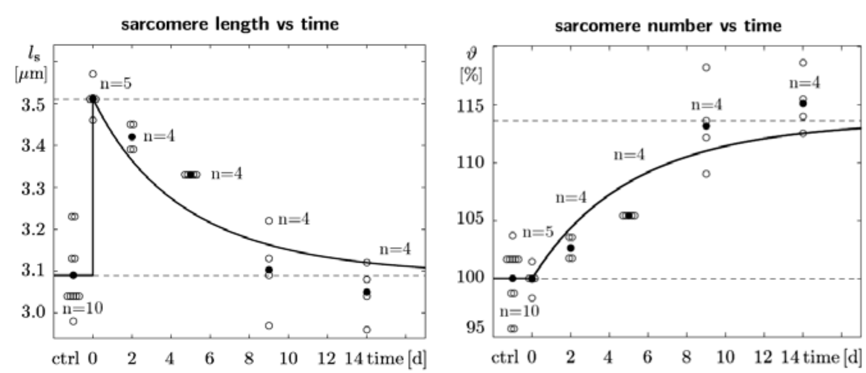


Figure 2. Stretching skeletal muscle. In a controlled limb lengthening model in rabbits, the radius and the ulna of the left forearm are lengthened by 4% inducing a stretch of $\lambda = 1.14$ in the extensor digitorum lateralis muscle. Chronic eccentric muscle growth through sarcomerogenesis is characterized in situ using light diffraction imaging. Adopted with permission from [33].

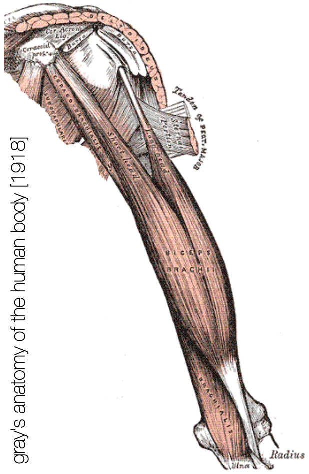
matano, tamai, kurokawa [1994], zöllner, abilez, böl, kuhl [2012]

stretching of extensor digitorum laterialis muscle



zöllner, abilez, böl, kuhl [2012]

example 02 – tendon tear



gray's anatomy of the human body [1918]

in contrast to limb lengthening, **tendon lengthening**, **tendon transfer**, and **tendon reattachment** after **tendon tear** are surgical procedures, which directly manipulate the muscle-tendon complex to correct posture or gait, and to improve or restore force generation. typically, these corrections are performed in a **single-step procedure**, which permits the muscle to regain its original architecture. recent studies suggest that a restoration of normal architecture and physiological function might be possible through a **gradual lengthening** of the musculotendinous unit when stretched at a rate of **1mm per day**. while we can sufficiently well approximate the short-term response to these surgical procedures by kinematic models, we are currently unable to predict their long-term behavior through chronic muscle adaptation.

stretching of biceps brachii muscle

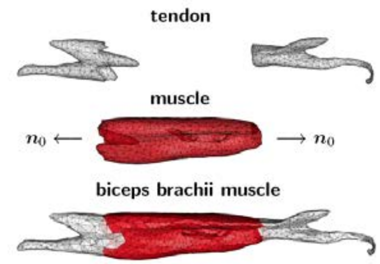
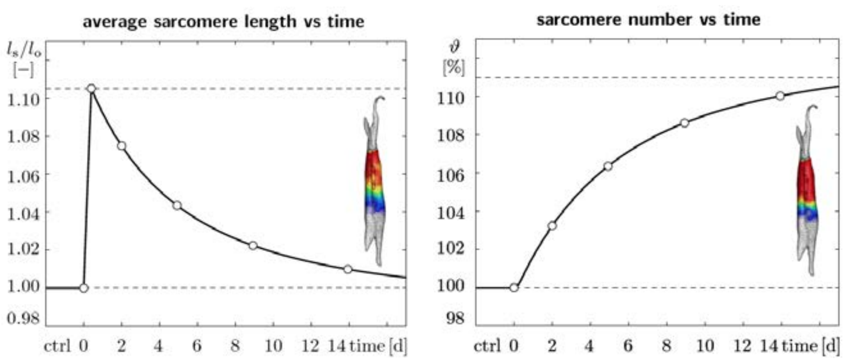


Figure 7. Biceps brachii muscle. The finite element model reconstructed from magnetic resonance images consists of 2,705 nodes and a total of 11,816 linear tetrahedral elements. The muscle, discretized by 9,393 elements (red), is attached to the elbow (left) and to the shoulder (right) through the distal and proximal biceps tendons, discretized by 2,423 elements (gray). The biceps brachii is a classical fusiform muscle with fibers $\boldsymbol{n}_0$ arranged in parallel bundles along its long axis [6].

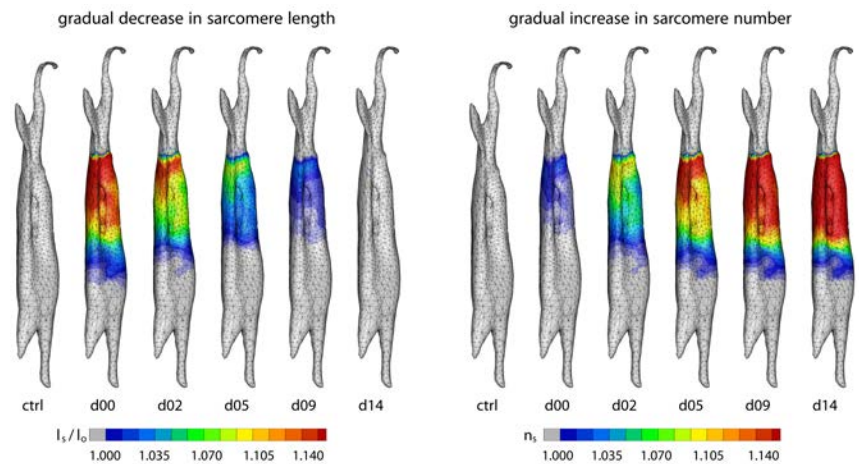
zöllner, abilez, böl, kuhl [2012]

serial sarcomere length vs time



zöllner, abilez, böl, kuhl [2012]

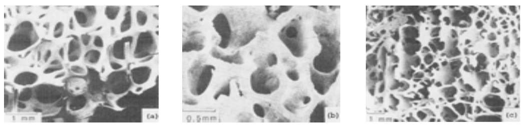
serial sarcomere length vs time



zöllner, abilez, böl, kuhl [2012]

density growth at constant volume

- free energy $\psi_0 = \left[\frac{\rho_0}{\rho_0^*}\right]^n \psi_0^{\mathrm{neo}}(\boldsymbol{F})$
- stress $\boldsymbol{P} = \left[\frac{\rho_0}{\rho_0^*}\right]^n \boldsymbol{P}^{\mathrm{neo}}(\boldsymbol{F})$
- mass flux $\boldsymbol{R} = R_0 \, \nabla_X \rho_0$
- mass source $\mathcal{R}_0 = \left[\frac{\rho_0}{\rho_0^*}\right]^{-m} \psi_0(\boldsymbol{F}) - \psi_0^*$

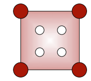


constitutive coupling of growth and deformation

gibson & ashby [1999]

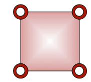
density growth

staggered solution - integration point based



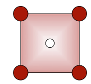
weinans, huiskes & grootenboer [1992], harrigan & hamilton [1992],, [1994], jacobs, levenston, beaupré,simo & carter [1995]

simultaneous solution - node point based



jacobs, levenston, beaupré,simo & carter [1995], fischer, jacobs, levenston & carter [1997], nackenhorst [1997], levenston [1997]]

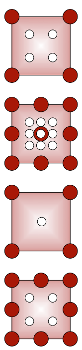
sequential solution - element based



huiskes, weinans, grootenboer, dalstra, fudala & slooff [1987], carter, orr, fhyrie [1989], beaupré, orr & carter [1990], weinans, huiskes & grootenboer [1992], [1994], jacobs, levenston, beaupré, simo & carter [1995], huiskes [2000], carter & beaupré [2001]

density growth - finite element method

integration point based solution of growth equation

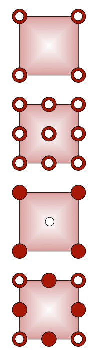


- loop over all time steps
  - global newton iteration
    - loop over all elements
      - loop over all quadrature points
        - local newton iteration to determine $\rho_{0\,n+1}$
      - determine element residual & partial derivative
    - determine global residual and iterational matrix
  - determine φ_{n+1}
- determine state of biological equilibrium

density ρ_0 as internal variable

density growth - finite element method

node point based solution of growth equation



- loop over all time steps
  - global newton iteration
    - loop over all elements
      - loop over all quadrature points
        - evaulate balance of mass and momentum
      - determine element residuals & partial derivatives
    - determine global residuals and iterational matrices
  - determine $\rho_{0\,n+1}$ and φ_{n+1}
- determine state of biological equilibrium

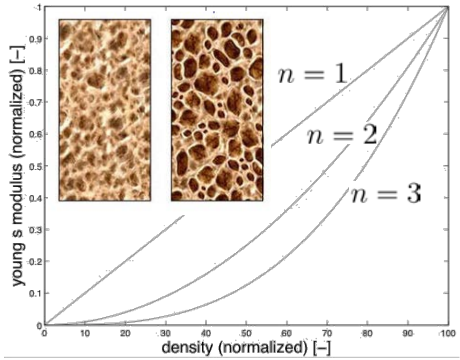
density ρ_0 as nodal degree of freedom

density growth - finite element method

neo hooke'ian elasticity of bone as a cellular material

free energy $\psi_0 = \left[\frac{\rho_0}{\rho_0^*}\right]^n \psi_0^{\text{neo}}(\boldsymbol{F})$

$\text{E} = 3.790\, \rho_0^3 \text{ MPa} \quad \rho_0 \text{ in g/cm}^3$



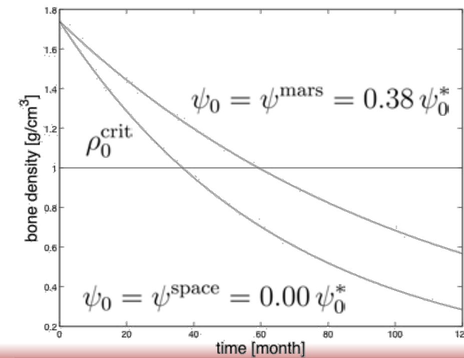
carter & hayes [1977]

example – bone loss in space

density growth - bone loss in space

$$\text{D}_t\rho_0 = c\,\rho_0\left[\,\frac{\psi_0}{\psi_0^*} - 1\,\right] \qquad \text{D}_t\rho_0 = \frac{1}{\Delta t}\left[\rho_0^{\text{n+1}} - \rho_0^{\text{n}}\right]$$

$$\rho_0^{\text{n+1}} = \rho_0^{\text{n}} + c\,\rho_0^{\text{n}}\left[\,\frac{\psi_0}{\psi_0^*} - 1\,\right]\Delta t \qquad \rho_0(t_0) = 1.79\,\frac{\text{g}}{\text{cm}^3}$$

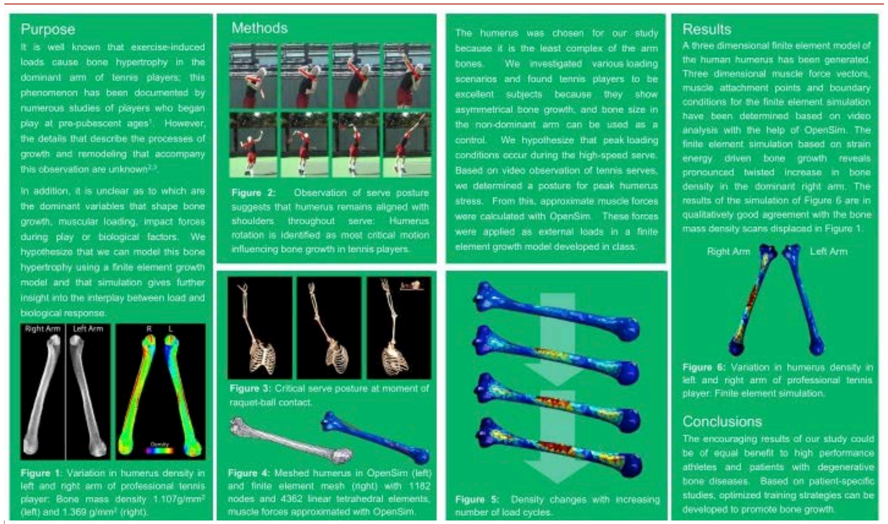


$\rho_0(36) = 1.0098$

$\rho_0(37) = 0.9947$

example - bone loss in space

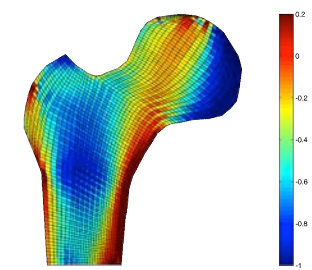
tennis player's arm



example - tennis player's arm

functional adaptation of proxima femur

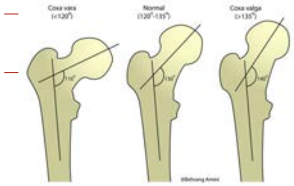
$\text{D}_t\rho_0 = \mathcal{R}_0 \qquad \mathcal{R}_0 = \left[\frac{\rho_0}{\rho_0^*}\right]^{-m}\psi_0 - \psi_0^*$



the density develops such that the tissue can just support the given mechanical load

example - growing bone

femoral neck deformity

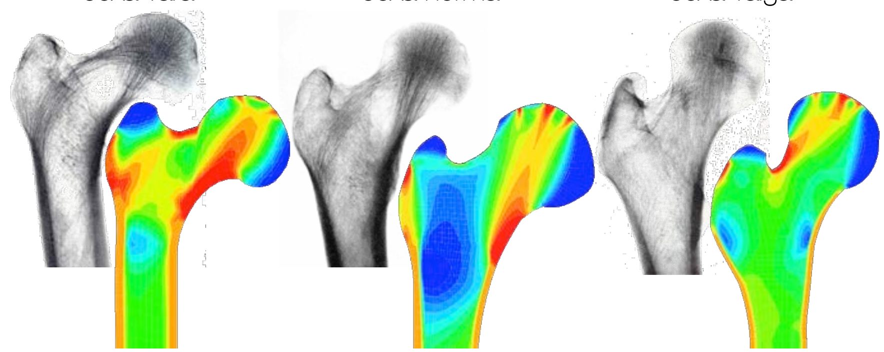


the femoral neck normally forms an angle of 120-135 degrees with the shaft of the bone. this acts as the lever in easing the action of the muscles around the hip joint. an increase or decrease in this angle beyond the normal limits causes improper action of muscles, and interferes with walking. an increase in the angle beyond 135 degrees is called **coxa valga** or outward curvature of the hip joint. a decrease in the angle below 120 degrees is called **coxa vara** or inward curvature of the hip joint.

example - femoral neck deformity

simulation vs. x-ray scans

coxa vara coxa norma coxa valga



excellent agreement of simulation and x-ray pattern

pauwels [1973], balle [2004], kuhl & balle [2005]

example - femoral neck deformity

total hip replacement vs hip resurfacing

- about 120,000 artificial hip replacements in us per year
- aseptic loosening caused by adaptive bone remodeling
- goal prediction of dredisctribution of bone density

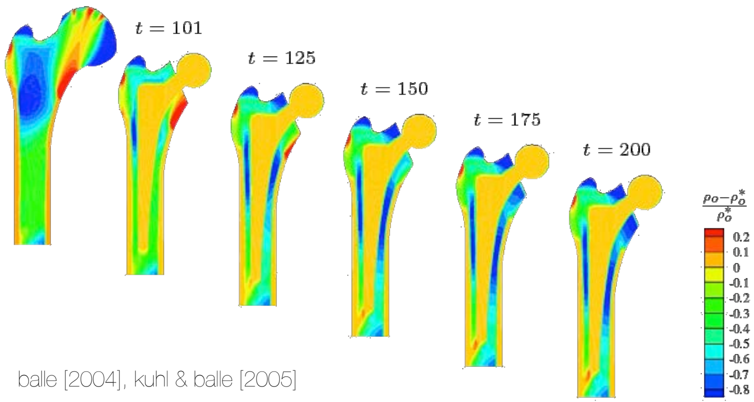
example - hip replacement

total hip replacement

total hip replacement is a surgical procedure in which the hip joint is replaced by a prostetic implant. a total hip replacement consists of replacing both the acetabulum and the femoral head. hip replacement is currently the most successful and reliable orthopaedic operation. risks and complications include aseptic loosening, dislocation, and pain.in the long term, many problems relate to **bone resorption and subsequent loosening** or fracture often requiring revision surgery.

example - hip replacement

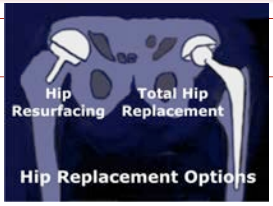
conventinal total hip replacement



balle [2004], kuhl & balle [2005]

stress shielding • bone resorption • implant loosening

hip resurfacing



hip resurfacing is a surgical procedure which has been developed as an intervention alternative to total hip replacement. the potential advantages of hip resurfacing include **less bone removal**, a potentially lower number of hip dislocations due to a relatively larger femoral head size, and possibly easier revision surgery for a subsequent total hip replacement device. the potential disadvantages are femoral neck fractures, aspectic loosening, and metal wear.

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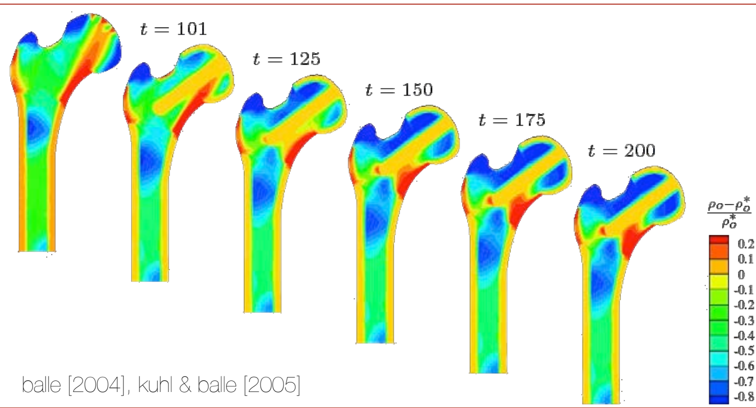
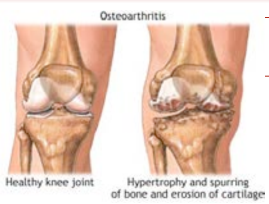
new birmingham hip resurfacing



balle [2004], kuhl & balle [2005]

improved ingrowth • anatomic situation • less resorption

osteoarthritis



osteoarthritis, also known as degenerative joint disease or osteoarthrosis, is a group of mechanical abnormalities involving degradation of joints, including articular cartilage and subchondral bone. it affects about 27 million people in the united states alone. symptoms may include joint pain, tenderness, stiffness, locking, and sometimes an effusion. a variety of causes, hereditary, developmental, metabolic, and mechanical, may initiate processes leading to loss of cartilage. when bone surfaces become less well protected by cartilage, bone may be exposed and damaged. treatment generally involves a combination of exercise, lifestyle modification, or, in severe cases,surgical joint replacement.

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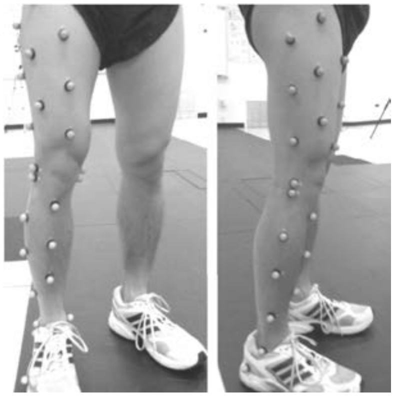
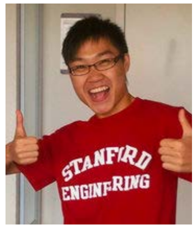
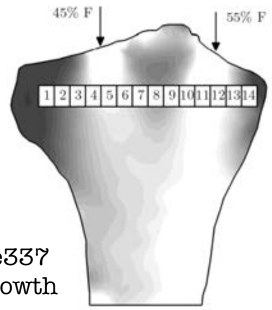
Computational modeling of bone density profiles in response to gait: A subject-specific approach

Henry Pang[1], Abhishek P. Shiwalkar[1], Chris M. Madormo[1], Rebecca E. Taylor[1], Thomas P. Andriacchi[1,2], Ellen Kuhl[1,3,4]







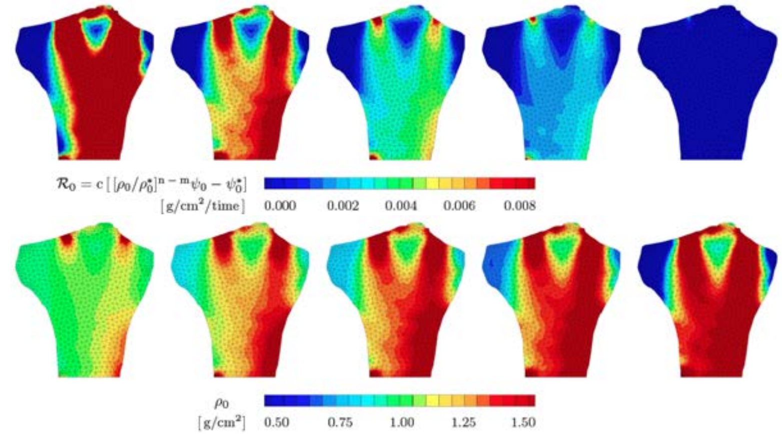
class project me337
mechanics of growth

trial	I	II	III	mean
max knee force [N]	552	549	579	560
max knee force [% BW]	94.9	94.4	99.4	96.2

pang, shiwalkar, madormo, taylor, andriacchi, kuhl [2012]

example – henry's knee

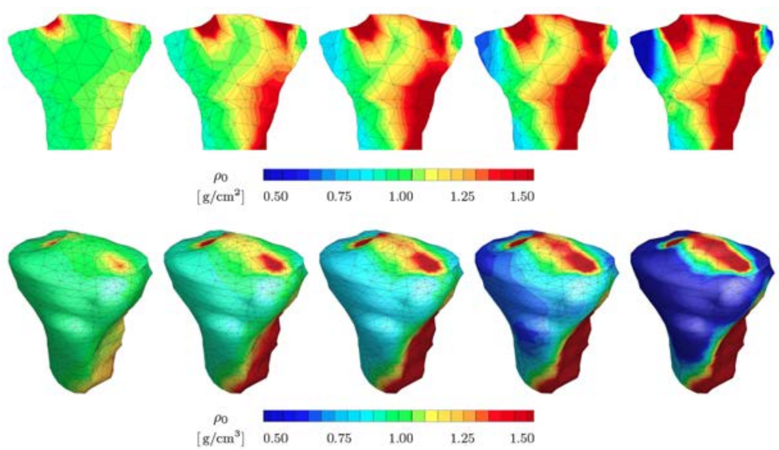
how does henry's bone grow?



pang, shiwalkar, madormo, taylor, andriacchi, kuhl [2012]

example – henry's knee

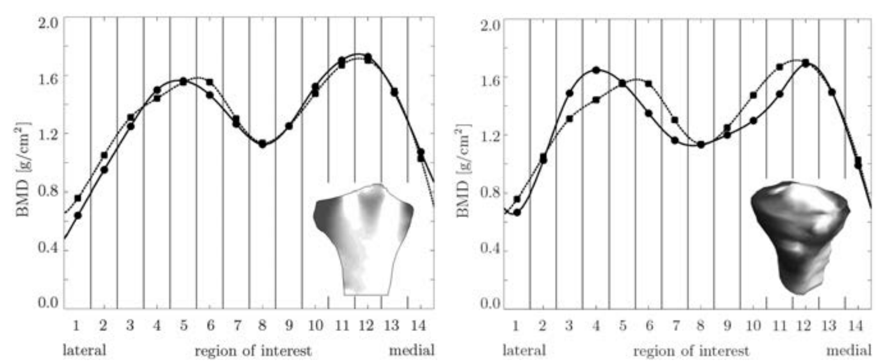
how does henry's bone grow?



pang, shiwalkar, madormo, taylor, andriacchi, kuhl [2012]

example – henry's knee

how predictive is the simulation?



pang, shiwalkar, madormo, taylor, andriacchi, kuhl [2012]

example – henry's knee