08 - basics constitutive equations - volume growth - growing tumors

day	date		topic
tue	jan	10	motivation - everything grows!
thu	jan	12	basics maths - notation and tensors
tue	jan	17	basic kinematics - large deformation and growth
thu	jan	19	kinematics - growing hearts
tue	jan	24	guest lecture - growing skin
thu	jan	26	guest lecture - growing leaflets
tue	jan	31	basic balance equations - closed and open systems
thu	feb	02	basic constitutive equations - growing tumors
tue	feb	07	volume growth - finite elements for growth
thu	feb	09	volume growth - growing arteries
tue	feb	14	volume growth - growing skin
thu	feb	16	volume growth - growing hearts
tue	feb	21	basic constitutive equations - growing bones
thu	feb	23	density growth - finite elements for growth
tue	feb	28	density growth - growing bones
thu	mar	01	everything grows! - midterm summary
tue	mar	06	midterm
thu	mar	08	remodeling - remodeling arteries and tendons
tue	mar	13	class project - discussion, presentation, evaluation
thu	mar	15	class project - discussion, presentation, evaluation
thu	mar	15	written part of final projects due

homework II - first draft of final project

due 02/16/12, 09:30am, 300-020

Late homework can be dropped off in a box in front of Durand 217. Please mark clearly with date and time @drop off. We will take off 1/10 of points for each 24 hours late, every 12pm after due date. This homework will count 10% towards your final grade.

problem 1 - kinematics of growth

The overall objective is this homework is to characterize the muscle fiber lengthening during growth. This is pretty straightforward if you solve the following substeps!

1.1 Determine three vectors $\mathrm{d}X_i$ that span the tetrahedron at baseline.

1.11 Determine the volume change $J^g = \det(F^g)$ and compare it with the small strain volume dilation $e^g = \mathrm{tr}(\epsilon^g)$. What does this imply in terms of tissue growth?

You can use MATLAB to solve the matrix and vector operations. If you choose to do so, you must deliver a printout of your MATLAB code with the homework. You can find additional details in the lecture notes from the fourth class.

problem 2 - shaping your research project

To structure your thoughts for your final project, read the attached paper by George M. Whitesides *"Writing a Paper"* as a guideline.

ADVANCED MATERIALS   ESSAY

Whitesides' Group: Writing a Paper**

By *George M. Whitesides**

1. What is a Scientific Paper?

A paper is an organized description of hypotheses, data and conclusions, intended to instruct the reader. Papers are a central part of research. If your research does not generate papers, it might just as well not have been done. "Interesting and unpublished" is equivalent to "non-existent".

Realize that your objective in research is to formulate and test hypotheses, to draw conclusions from these tests, and to teach these conclusions to others. Your objective is not to "collect data".

do *not* agree on the outline, any text is useless. Much of the *time* in writing a paper goes into the text; most of the *thought* goes into the organization of the data and into the analysis. It can be relatively efficient in time to go through several (even many) cycles of an outline before beginning to write text; writing many versions of the full text of a paper is slow.

All writing that I do—papers, reports, proposals (and, of course, slides for seminars)—I do from outlines. I urge you to learn how to use them as well.

2.1 Sketch a *bulleted outline* for your project. This does not need to be your final layout, it is just meant to organize your ideas. Identify the sections and subsections of your paper.

2.2.a If you plan to write a scientific paper, identify a key *hypothesis*. The purpose of the hypothesis is to provide focus throughout the manuscript. A good hypothesis is objectively testable, non-trivial, and specific. For example, you could hypothesize that cardiac growth in athletes is reversible and vanishes gradually upon detraining. If you plan a finite element analysis, a reasonable hypothesis might involve regional variations in density or volume growth in relation to strain, stress, shape or something similar.

2.2.b If you plan to write a review paper, it might be more difficult to *keep focus*. In one sentence, specify precisely which aspects of growth you want to review. Remember the characteristics of your last homework, i.e., type of tissue, type of growth, scale you look at, mechanical driving force, disease specific or training, etc.

2.3 Identify *three key references* for your work and at least *three additional references* that you consider relevant. If you work in a group identify *five key references* for your work and at least *five additional references*. Create a bibliography and submit it with this homework.

2.4 Identify a catchy *opening sentence*. This sentence is meant to catch the attention of the reader. If you plan on writing something disease related, this sentence should reflect the medical importance of your work. For example, this sentence can state the number of people affected, the health care cost involved, or the predicted growth of this disease. Provide a citation to back up your statement.

2.5 Summarize the *current knowledge* citing the literature you have listed in your bibliography file. This section will later be part of your Introduction section.

2.5.a If you plan to write a scientific paper, consider breaking the current knowledge section into two paragraphs, one on the biological nature and one mechanical modeling.

2.5.b If you plan to write a review paper, consider breaking the current knowledge section into two or three paragraphs for the individual aspects you plan to review and compare.
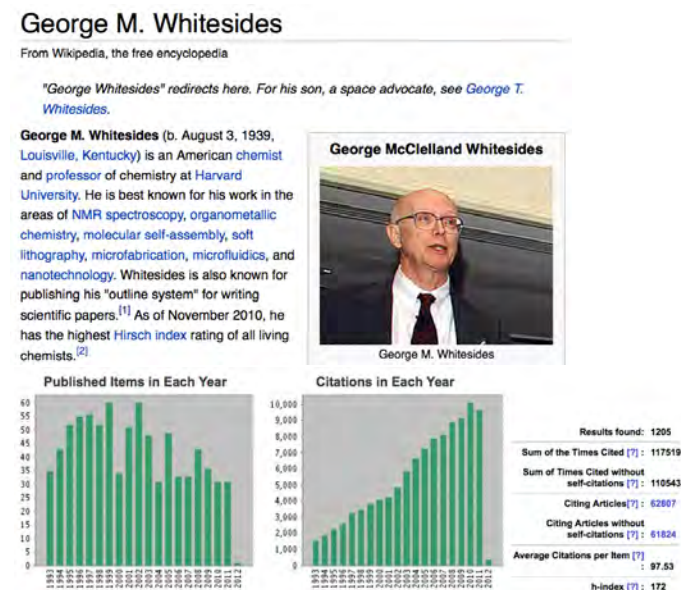
2.6 Create a schematic drawing that summarizes your project. The figures below show two samples of schematic drawings. If you like, you can draft this drawing by hand first. Ultimately, this figure will go into the introduction of your paper, to give the reader a quick overview about your work.
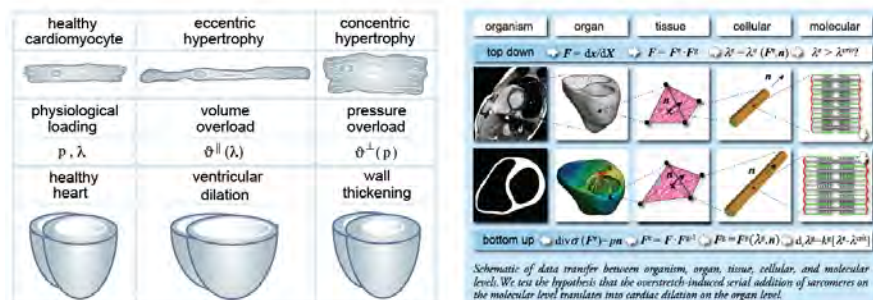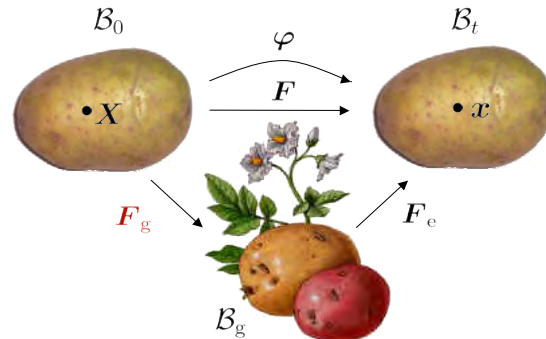
Although these sub-problems seem to require just a few words, put some effort into structuring your work - this will definitely pay off in the end.

George M. Whitesides
From Wikipedia, the free encyclopedia

"George Whitesides" redirects here. For his son, a space advocate, see *George T. Whitesides*.

George M. Whitesides (b. August 3, 1939, Louisville, Kentucky) is an American chemist and professor of chemistry at Harvard University. He is best known for his work in the areas of NMR spectroscopy, organometallic chemistry, molecular self-assembly, soft lithography, microfabrication, microfluidics, and nanotechnology. Whitesides is also known for publishing his "outline system" for writing scientific papers.[1] As of November 2010, he has the highest Hirsch index rating of all living chemists.[2]

George McClelland Whitesides

George M. Whitesides

Published Items in Each Year

Citations in Each Year

Results found: 1205
Sum of the Times Cited [?] : 117519
Sum of Times Cited without
self-citations [?] : 110543
Citing Articles[?] : 62807
Citing Articles without
self-citations [?] : 61824
Average Citations per Item [?]
: 97.53
h-index [?] : 172

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The Free Encyclopedia

kinematics of finite growth

$$\mathcal{B}_0 \qquad \varphi \qquad \mathcal{B}_t$$
$$\boldsymbol{F}$$
$$\bullet X \qquad \bullet x$$
$$\boldsymbol{F}_{\mathrm{g}} \qquad \boldsymbol{F}_{\mathrm{e}}$$
$$\mathcal{B}_{\mathrm{g}}$$

- 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]

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balance of mass of 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)
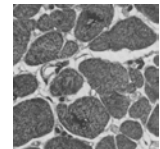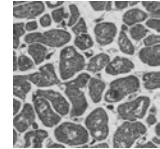
biological equilibrium

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

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generic balance equation of open systems

$$\boldsymbol{R} \qquad \partial \bar{\mathcal{B}} \qquad \boldsymbol{n}$$
$$\bar{\boldsymbol{T}}^{\mathrm{A}}$$
$$\mathcal{B} \quad \begin{matrix} \mathsf{A} \\ \mathsf{C} \quad \mathcal{R}_0 \\ \Gamma \end{matrix}$$

general format

A … balance quantity
$\boldsymbol{B}$ … flux $\quad \boldsymbol{B} \cdot \boldsymbol{n} = \bar{\boldsymbol{T}}^{\mathrm{A}}$
C … source
Γ … production
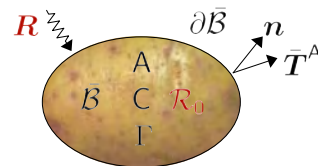
$$\mathrm{D}_t(\rho_0 \mathsf{A}) = \mathrm{Div}(\boldsymbol{B} + \mathsf{A} \otimes \boldsymbol{R}) + [\mathsf{C} + \mathsf{A}\mathcal{R}_0 - \nabla_X \mathsf{A} \cdot \boldsymbol{R} + \Gamma]$$

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constitutive equations

constitutive equations [kɒnˈstɪtuˌtɪv ɪˈkweɪʒəns] 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.**

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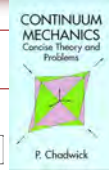
constitutive equations [kənˈstɪ.tu.tɪv ɪˈkweɪ.ʒəns] or equations of state bring in the **charac-terization of particular materials** within continuum mechanics. mathematically, the purpose of these relations is to supply connections between kinematic, mechanical and thermal fields. physically, constitu-tive equations represent the various forms of **idealized material response** which serve as **models** of the behavior of actual substances.

chadwick "continuum mechanics" [1976]

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tensor analysis - these derivatives might be handy

$$\{\bullet \otimes \circ\}_{ijkl} = \{\bullet\}_{ij}\{\circ\}_{kl}$$
$$\{\bullet \overline{\otimes} \circ\}_{ijkl} = \{\bullet\}_{ik}\{\circ\}_{jl}$$
$$\{\bullet \underline{\otimes} \circ\}_{ijkl} = \{\bullet\}_{il}\{\circ\}_{jk}$$

$$\frac{\partial \boldsymbol{F}}{\partial \boldsymbol{F}} = \boldsymbol{I}\,\overline{\otimes}\,\boldsymbol{I} \qquad \frac{\partial F_{ij}}{\partial F_{kl}} = \delta_{ik}\,\delta_{jl}$$

$$\frac{\partial \boldsymbol{F}^{-1}}{\partial \boldsymbol{F}} = -\boldsymbol{F}^{-1}\,\overline{\otimes}\,\boldsymbol{F}^{-t} \qquad \frac{\partial F_{ij}^{-1}}{\partial F_{kl}} = -F_{ik}^{-1}\,F_{lj}^{-1}$$

$$\frac{\partial \boldsymbol{F}^{t}}{\partial \boldsymbol{F}} = \boldsymbol{I}\,\underline{\otimes}\,\boldsymbol{I} \qquad \frac{\partial F_{ji}}{\partial F_{kl}} = \delta_{il}\,\delta_{jk}$$

$$\frac{\partial \boldsymbol{F}^{-t}}{\partial \boldsymbol{F}} = -\boldsymbol{F}^{-t}\,\underline{\otimes}\,\boldsymbol{F}^{-1} \qquad \frac{\partial F_{ji}^{-1}}{\partial F_{kl}} = -F_{li}^{-1}\,F_{jk}^{-1}$$

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tensor analysis - these derivatives might be handy

$$\frac{\partial \det(\boldsymbol{F})}{\partial \boldsymbol{F}} = \det(\boldsymbol{F})\,\boldsymbol{F}^{-t} \qquad \frac{\partial \ln(\det(\boldsymbol{F}))}{\partial \boldsymbol{F}} = \boldsymbol{F}^{-t}$$

$$\frac{\partial \det(\boldsymbol{F}^{-1})}{\partial \boldsymbol{F}} = -\frac{1}{\det(\boldsymbol{F})}\,\boldsymbol{F}^{-t} \qquad \frac{\partial \ln(\det(\boldsymbol{F})^{-1})}{\partial \boldsymbol{F}} = -\boldsymbol{F}^{-t}$$

$$\frac{\partial \ln(\det(\boldsymbol{F}))}{\partial(\det(\boldsymbol{F}))} = \frac{1}{\det(\boldsymbol{F}))} \qquad \frac{\partial \ln^2(\det(\boldsymbol{F}))}{\partial \boldsymbol{F}} = 2\ln(\det(\boldsymbol{F}))\boldsymbol{F}^{-t}$$

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neo hooke'ian elasticity

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

- definition of stress
$$\boldsymbol{P}^{\text{neo}} = \mathrm{D}_F\psi_0^{\text{neo}}$$
$$= \tfrac{1}{2}\lambda_0\,2\ln(\det\boldsymbol{F})\boldsymbol{F}^{-t} + \tfrac{1}{2}\mu_0\,2\,\boldsymbol{F} - \mu_0\boldsymbol{F}^{-t}$$
$$= \mu_0\,\boldsymbol{F} + [\,\lambda_0\ln(\det(\boldsymbol{F})) - \mu_0\,]\boldsymbol{F}^{-t}$$

- definition of tangent operator
$$\boldsymbol{A}^{\text{neo}} = \mathrm{D}_{FF}\psi_0^{\text{neo}} = \mathrm{D}_F\boldsymbol{P}^{\text{neo}}$$
$$= \lambda_0\boldsymbol{F}^{-t}\otimes\boldsymbol{F}^{-t} + \mu_0\boldsymbol{I}\overline{\otimes}\boldsymbol{I}$$
$$+ [\,\mu_0 - \lambda_0\ln(\det(\boldsymbol{F}))\,]\,\boldsymbol{F}^{-t}\underline{\otimes}\boldsymbol{F}^{-1}$$
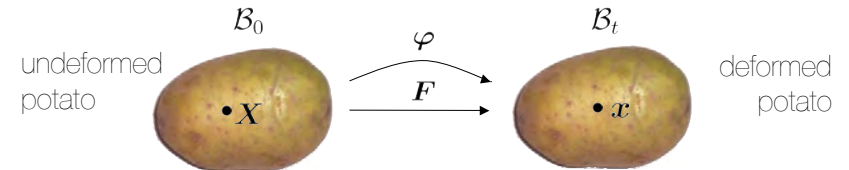
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neo hooke'ian elasticity

- free energy
$$\psi_0^{\mathrm{neo}} = \tfrac{1}{2}\,\lambda_0 \ln^2(\det(F_{ij}))$$
$$+ \tfrac{1}{2}\,\mu_0[\,F_{ij}F_{ij} - n^{\dim} - 2\ln(\det(F_{ij}))\,]$$

- definition of stress
$$P_{ij}^{\mathrm{neo}} = \mathrm{D}_{F_{ij}}\psi_0^{\mathrm{neo}}$$
$$= \tfrac{1}{2}\,\lambda_0\,2\ln(\det F_{ij})F_{ji}^{-1} + \tfrac{1}{2}\mu_0\,2\,F_{ij} - \mu_0 F_{ji}^{-1}$$
$$= \mu_0\,F_{ij} + [\,\lambda_0\ln(\det(F_{ij})) - \mu_0\,]F_{ji}^{-1}$$

- definition of tangent operator
$$\mathsf{A}_{ijkl}^{\mathrm{neo}} = \mathrm{D}_{F_{ij}F_{kl}}\psi_0^{\mathrm{neo}} = \mathrm{D}_{F_{kl}}P_{ij}^{\mathrm{neo}}$$
$$= \lambda_0 F_{ji}^{-1}\,F_{lk}^{-1} + \mu_0 I_{ik}\,I_{jl}$$
$$+[\mu_0 - \lambda_0\ln(\det(F_{ij}))]\,F_{li}^{-1}\,F_{jk}^{-1}$$

constitutive equations   17

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neo hooke'ian elasticity

$$\mathcal{B}_0 \qquad \varphi \qquad \mathcal{B}_t$$

undeformed potato $\bullet X$ F $\bullet x$ deformed potato

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

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

constitutive equations   18

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neo hooke'ian elasticity

$$\mathcal{B}_0 \qquad \varphi \qquad \mathcal{B}_t$$

undeformed potato $\bullet X$ F $\bullet x$ mashed potatoes
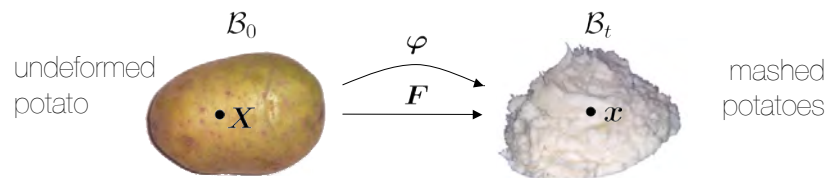
- free energy
$$\psi^{\mathrm{neo}} = \tfrac{1}{2}\,\lambda \ln^2(\det(\boldsymbol{F}))$$
$$+ \tfrac{1}{2}\,\mu[\,\boldsymbol{F}^{\mathrm{t}}\cdot\boldsymbol{F}:\boldsymbol{I} - n^{\dim} - 2\ln(\det(\boldsymbol{F}))\,]$$

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

- remember! mashing potatoes is not an elastic process!

constitutive equations   19

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neo hooke'ian elasticity

$$\mathcal{B}_0 \qquad \varphi \qquad \mathcal{B}_t$$

undeformed potato $\bullet X$ F $\bullet x$ deformed potato
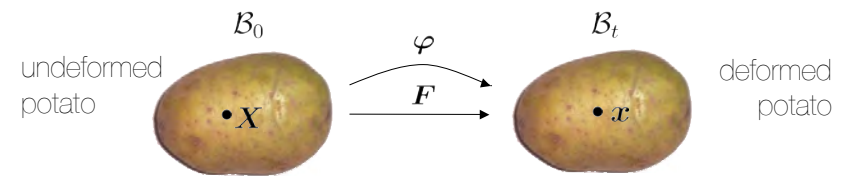
- free energy
$$\psi_0^{\mathrm{neo}} = \tfrac{1}{2}\,\lambda_0 \ln^2(\det(\boldsymbol{F}))$$
$$+ \tfrac{1}{2}\,\mu_0[\,\boldsymbol{F}^{\mathrm{t}}\cdot\boldsymbol{F}:\boldsymbol{I} - n^{\dim} - 2\ln(\det(\boldsymbol{F}))\,]$$

- large strain - lamé parameters and bulk modulus
$$\lambda = \frac{E\nu}{[1+\nu][1-2\nu]} \qquad \mu = \frac{E}{2[1+\nu]} \qquad \kappa = \frac{E}{3[1-2\nu]}$$

- small strain - young's modulus and poisson's ratio
$$E = 3\kappa[1-2\nu] \qquad \nu = \frac{3\kappa-2\mu}{2[3\kappa+\mu]}$$
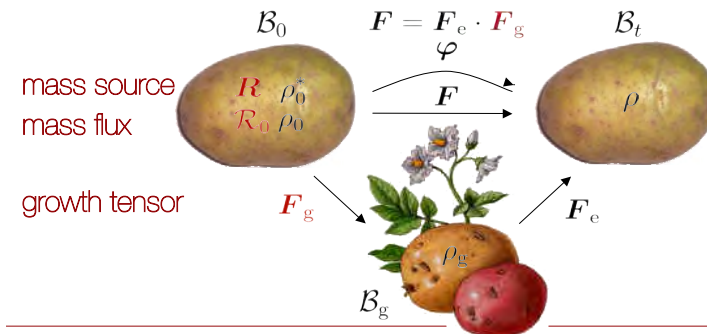
constitutive equations   20

neo hooke'ian elasticity - cellular tissues

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

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

carter & hayes [1977]

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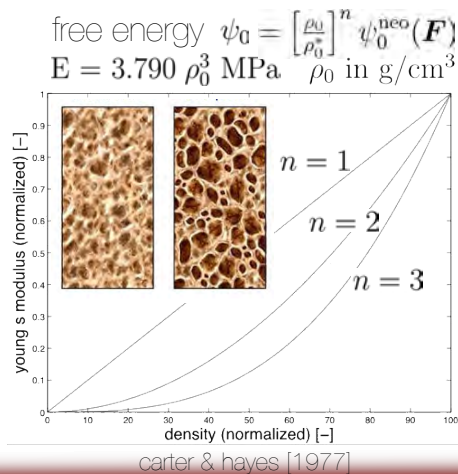
additional constitutive equations for volume growth

$\mathcal{B}_0 \qquad \boldsymbol{F} = \boldsymbol{F}_\mathrm{e} \cdot \boldsymbol{F}_\mathrm{g} \qquad \mathcal{B}_t$

φ

mass source

mass flux

$\boldsymbol{R} \quad \rho_0^+$

$\mathcal{R}_0 \quad \rho_0$

$\boldsymbol{F}$

ρ

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

ρ_g

$\mathcal{B}_\mathrm{g}$

multiplicative decomposition - but what is $\boldsymbol{F}_\mathrm{g}$?

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

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volume growth at constant density

- free energy $\quad \psi_\mathrm{a} = \psi_0^{\mathrm{neo}}(\boldsymbol{F}_\mathrm{e})$
- stress $\qquad \boldsymbol{P}_\mathrm{e} = \boldsymbol{P}_\mathrm{e}^{\mathrm{neo}}(\boldsymbol{F}_\mathrm{e})$
- growth tensor $\boldsymbol{F}_\mathrm{g} = \vartheta\,\boldsymbol{I} \quad \mathrm{D}_t\vartheta = k_\vartheta(\vartheta)\,\mathrm{tr}(\boldsymbol{C}_\mathrm{e} \cdot \boldsymbol{S}_\mathrm{e})$

  growth function   pressure
- mass source $\quad \mathcal{R}_0 = 3\,\rho_0\vartheta^2\mathrm{D}_t\vartheta$

  increase in mass
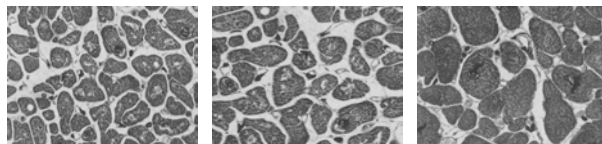
kinematic coupling of growth and deformation

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

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volume growth - cylindrical tumor

ductal carcinoma is a very common type of breast cancer in women. infiltrating ductal carcinoma refers to the development of invasive cancer cells within the milk ducts of the breast. it accounts for 80% of all types of breast cancer. on a mammography, it is usually visualized as a mass with fine spikes radiating from the edges, and small microcalcification may be seen as well. on physical examination, the lump usually feels hard or firm. on microscopic examination, the cancerous cells invade and replace the surrounding normal tissue inside the breast. the subtypes with histology of mucinous, papillary, cribriform, and tubular carcinomas have a better prognosis, longer survival, and lower recurrence rates Than those with histology like signet-ring cell or inflammatory carcinoma or carcinoma with sarcomatoid metaplasia.
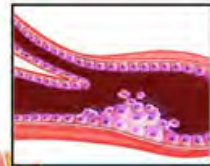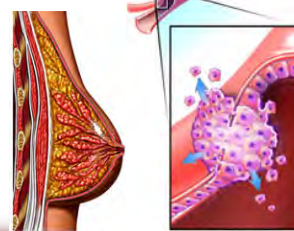
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normal cells grow and multiply at a specific rate. cells that grow and multiply without stopping are called cancerous or malignant. however, they are not detectable when they first start growing.

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 25

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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
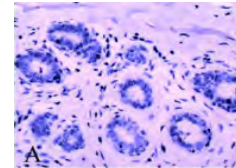
normal ductal epithelial cells (negative)
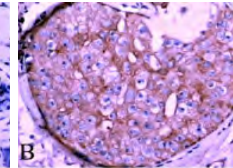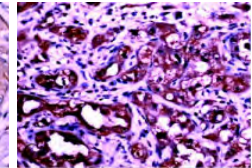
tumor cells of ductal carcinoma (positive)

invasive ductal carcinoma cells (strongly positive)

kinematic coupling of growth and deformation

example - breast cancer 26

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- homogeneous deformation inside a rigid cylinder

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

- deformation gradient

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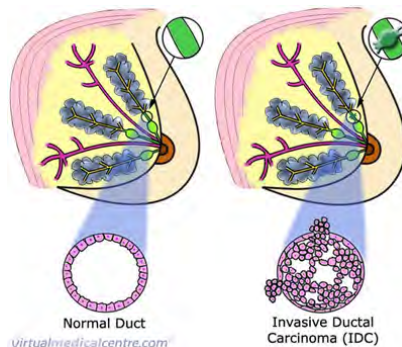
Normal Duct

Invasive Ductal Carcinoma (IDC)

virtualmedicalcentre.com

kinematic coupling of growth and deformation

example - breast cancer 27

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- free energy $\quad \psi_{\mathrm{a}} = \psi_0^{\mathrm{bko}}(\boldsymbol{F}_{\mathrm{e}}) = \frac{1}{2}\mu[[I - 3] - \frac{2}{q}[III^{q/2} - 1]]$
- stress $\quad \boldsymbol{P}_{\mathrm{e}} = \boldsymbol{P}_{\mathrm{e}}^{\mathrm{bko}}(\boldsymbol{F}_{\mathrm{e}}) = \frac{1}{J_{\mathrm{e}}}\mu[-J_{\mathrm{e}}^{q}\boldsymbol{F}_{\mathrm{e}}^{-\mathrm{t}} + \boldsymbol{F}_{\mathrm{e}}] \cdot \boldsymbol{F}_{\mathrm{g}}^{-\mathrm{t}}$
- growth tensor $\boldsymbol{F}_{\mathrm{g}} = \vartheta\,\boldsymbol{I} \quad \vartheta(t) = \exp(\alpha\,t/3)$
- deformation $\quad x = X \qquad y = Y \qquad z = \lambda Z$

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 28

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$$F = \nabla_X \varphi$$

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

$$F_g = \vartheta\, I$$

$$F_g = \begin{bmatrix} \vartheta & 0 & 0 \\ 0 & \vartheta & 0 \\ 0 & 0 & \vartheta \end{bmatrix} \qquad \mathcal{B}_g$$

$$F_e = F \cdot F_g^{-1}$$

$$F_e = \begin{bmatrix} \frac{1}{\vartheta} & 0 & 0 \\ 0 & \frac{1}{\vartheta} & 0 \\ 0 & 0 & \frac{\lambda}{\vartheta} \end{bmatrix}$$

ambrosi & mollica [2002]

example - breast cancer   29

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cancer cells   duct wall

- stress $\qquad \sigma_e = \begin{bmatrix} \sigma_{xx} & 0 & 0 \\ 0 & \sigma_{yy} & 0 \\ 0 & 0 & \sigma_{zz} \end{bmatrix}$

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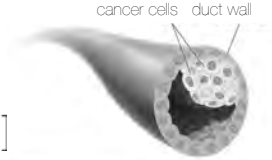
$$\sigma_{zz} = \mu\, \frac{\vartheta^3}{\lambda} \left[\frac{\lambda^2}{\vartheta^2} - \left[\frac{\lambda}{\vartheta^3} \right]^q \right]$$

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

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

- growth induced stress σ_{xx} on tumor wall

$$\sigma_{xx} = \mu \left[\vartheta^{2q/[2-q]} - \vartheta^{[4-4q]/[2-q]} \right]$$
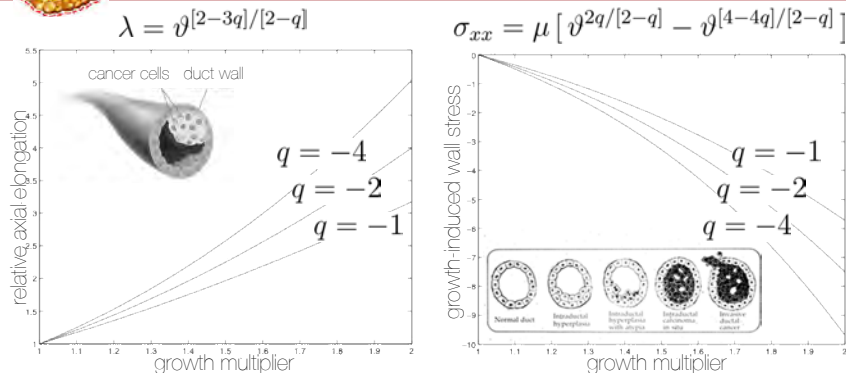
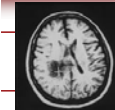ambrosi & mollica [2002]

example - breast cancer   30

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

cancer cells   duct wall

(left plot, relative axial elongation vs growth multiplier)
$q = -4$
$q = -2$
$q = -1$

(right plot, growth-induced wall stress vs growth multiplier)
$q = -1$
$q = -2$
$q = -4$

Normal duct | Intraductal hyperplasia | Intraductal hyperplasia with atypia | Intraductal calcinoma in situ | ductal cancer

tumor pressure on duct walls increases with growth

ambrosi & mollica [2002]

example - breast cancer   31
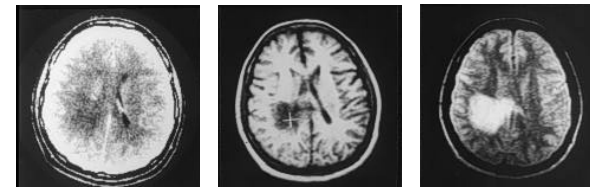
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model assumptions
- tumor model - inhomogeneous growth of a sphere
- inhomogeneity - residual stress even in the absense of applied loads
- assumption - spherical symmetry
- strategy - solve for deformation that satisfies equi'm and boundary cond's

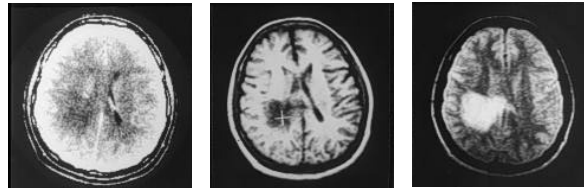**kinematic coupling of growth and deformation**

ambrosi & mollica [2002]

example - tumor growth   32

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- free energy $\quad \psi_0 = \psi_0^{\text{bko}}(\boldsymbol{F}_{\text{e}}) = \frac{1}{2}\mu[[I - 3] - \frac{2}{q}[III^{q/2} - 1]]$
- stress $\quad\quad \boldsymbol{P}_{\text{e}} = \boldsymbol{P}_{\text{e}}^{\text{bko}}(\boldsymbol{F}_{\text{e}}) = \frac{1}{J_{\text{e}}}\mu[-J_{\text{e}}^q \boldsymbol{F}_{\text{e}}^{-\text{t}} + \boldsymbol{F}_{\text{e}}] \cdot \boldsymbol{F}_{\text{g}}^{-\text{t}}$
- growth tensor $\boldsymbol{F}_{\text{g}} = \vartheta\,\boldsymbol{I} \quad \vartheta(R) = \frac{\alpha}{R}\sinh(k\,R)$
- deformation $\quad r = \lambda(R) \quad \theta = \Theta \quad \phi = \Phi$

kinematic coupling of growth and deformation

ambrosi & mollica [2002]

example - tumor growth　　33

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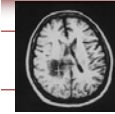
$$\boldsymbol{F} = \nabla_X \varphi$$

$$\mathcal{B}_0 \quad \boldsymbol{F} = \begin{bmatrix} \frac{\partial \lambda}{\partial R} & 0 & 0 \\ 0 & \frac{\lambda}{R} & 0 \\ 0 & 0 & \frac{\lambda}{R} \end{bmatrix} \quad \mathcal{B}_t$$
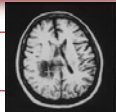
$$\boldsymbol{F}_{\text{g}} = \vartheta\,\boldsymbol{I}$$

$$\boldsymbol{F}_{\text{g}} = \begin{bmatrix} \vartheta & 0 & 0 \\ 0 & \vartheta & 0 \\ 0 & 0 & \vartheta \end{bmatrix} \quad \mathcal{B}_{\text{g}}$$

$$\boldsymbol{F}_{\text{e}} = \boldsymbol{F} \cdot \boldsymbol{F}_{\text{g}}^{-1}$$

$$\boldsymbol{F}_{\text{e}} = \begin{bmatrix} \frac{1}{\vartheta}\frac{\partial \lambda}{\partial R} & 0 & 0 \\ 0 & \frac{\lambda}{\vartheta R} & 0 \\ 0 & 0 & \frac{\lambda}{\vartheta R} \end{bmatrix}$$
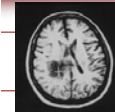
ambrosi & mollica [2002]

example - tumor growth　　34

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- stress $\quad \boldsymbol{P}_{\text{e}} = \begin{bmatrix} P_{RR} & 0 & 0 \\ 0 & P_{\Theta\Theta} & 0 \\ 0 & 0 & P_{\Phi\Phi} \end{bmatrix}$

$$P_{RR} = \mu\,\vartheta\left[\frac{\partial \lambda}{\partial R} - J_{\text{e}}^q\,\vartheta^2\left[\frac{\partial \lambda}{\partial R}\right]^{-1}\right]$$

$$P_{\Theta\Theta} = P_{\Phi\Phi} = \mu\,\vartheta\left[\frac{\lambda}{R} - J_{\text{e}}^q\,\vartheta^2\frac{R}{\lambda}\right]$$

$$J_{\text{e}} = \frac{\partial \lambda}{\partial R}\frac{\lambda^2}{\vartheta^3 R^2}$$

- balance of momentum $\quad \dfrac{dP_{RR}}{dR} + \dfrac{2}{R}[P_R R - P_{\Theta\Theta}] = 0$

- bc's $\quad \lambda(R = 0) = 0 \quad P_{RR}(R = \bar{R}) = 0$
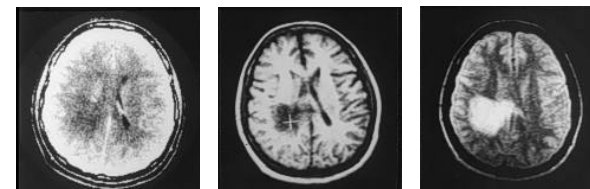
ambrosi & mollica [2002]

example - tumor growth　　35

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ordinary differential eqn of 2nd order in λ 2B solved numerically

$$\frac{\partial^2 \lambda}{\partial R^2} = \frac{\frac{2}{R}\left[\frac{1}{R} + \frac{\vartheta^2 J_{\text{e}}^q [1-q]}{\lambda\,\partial\lambda/\partial R}\right][\lambda - \frac{\partial \lambda}{\partial R}R] - \frac{1}{\vartheta}\left[\frac{\partial \lambda}{\partial R} - \frac{3\vartheta^2 J_{\text{e}}^q [1-q]}{\partial\lambda/\partial R}\frac{\partial \vartheta}{\partial R}\right]}{1 + \frac{\vartheta^2 J_{\text{e}} [1-q]}{[\partial\lambda/\partial R]^2}}$$
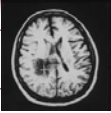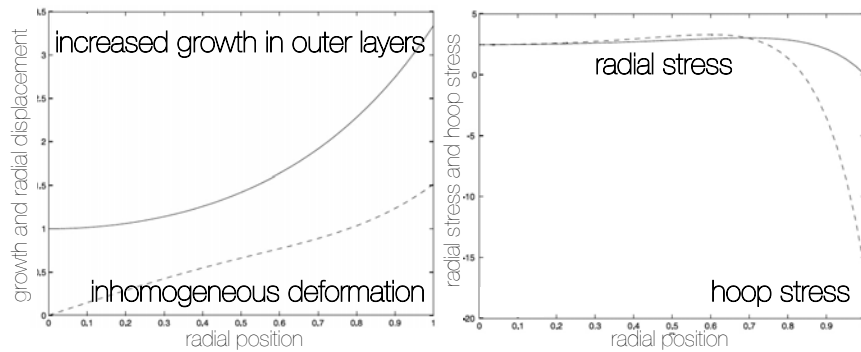

kinematic coupling of growth and deformation

ambrosi & mollica [2002]

example - tumor growth　　36

increased growth in outer layers

radial stress

growth and radial displacement

radial stress and hoop stress

inhomogeneous deformation

hoop stress

radial position

radial position

hoop stress tensile inside / compressive outside

ambrosi & mollica [2002]

example - tumor growth   37