

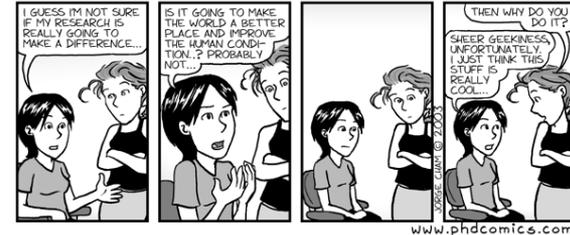
mechanics of growth

me 337



ellen kuhl
mechanical engineering
stanford university

01 - motivation -
everything grows!



01 - introduction

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... what we do ...



kinematic equations for finite growth

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



balance equations for open systems

$$D_t \rho_0 = \text{Div}(\mathbf{R}) + \mathcal{R}_0$$

$$\rho_0 D_t \mathbf{v} = \text{Div}(\mathbf{P}) + \mathbf{b}_0$$



constitutive equations for living tissues

$$\mathbf{P} = \mathbf{P}(\rho_0, \mathbf{F}, \mathbf{F}_g)$$



fe analyses for biological structures

continuum- & computational biomechanics

... why we do what we do ...



kinematic equations for finite growth

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fe analyses for biological structures

... because biological structures are ...

... what we do ...

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... what we do ...

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... why we do what we do ...



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fe analyses for biological structures



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... what we do ...

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... why we do what we do ...



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fe analyses for biological structures



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... what we do ...

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... why we do what we do ...



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fe analyses for biological structures



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... what we do ...

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... why we do what we do ...



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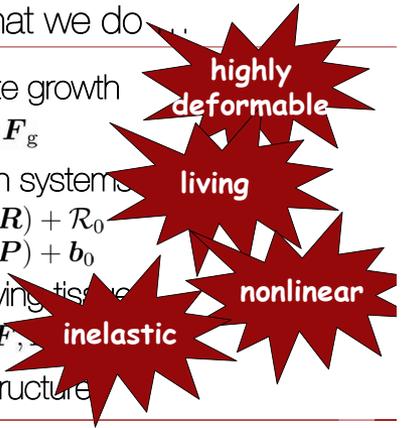


constitutive equations for living tissues

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fe analyses for biological structures



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... why we do what we do ...



kinematic equations for finite growth

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balance equations for open systems

$$D_{t_0} \rho_0 = \text{Div}(\mathbf{J}) + \mathcal{R}_0$$



constitutive equations

$$\mathbf{P} = \mathbf{P}(\rho_0, \mathbf{F}, \dots)$$



fe analyses for biological structures

highly deformable

living

anisotropic

nonlinear

inelastic

... because biological structures are ...

... what we do ...

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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**

introduction

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... why we do what we do ...



kinematic equations for finite growth

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



balance equations for open systems

$$D_{t_0} \rho_0 = \text{Div}(\mathbf{J}) + \mathcal{R}_0$$



constitutive equations

$$\mathbf{P} = \mathbf{P}(\rho_0, \mathbf{F}, \dots)$$



fe analyses for biological structures

highly deformable

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nonlinear

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inhomogeneous

... because biological structures are ...

... what we do ...

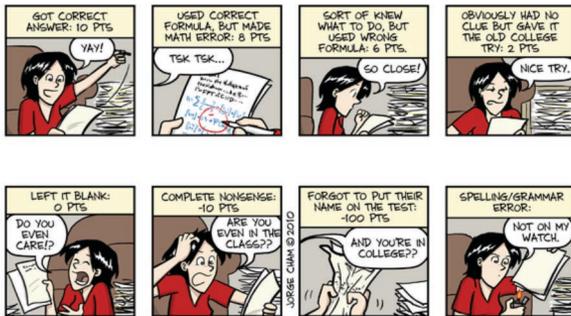
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me 337 - syllabus

day	date	topic
tue	sep 21	motivation - everything grows!
thu	sep 23	basics and maths - notation and tensors
tue	sep 28	class project 07 - growth of tennis player arms
thu	sep 30	guided reading - no class
tue	oct 05	basics and mechanics - kinematics and balance equations of growth
thu	oct 07	guided reading - no class
tue	oct 12	density growth - growing bones
thu	oct 14	density growth - finite elements for growth / theory
tue	oct 19	density growth - finite elements for growth / matlab
thu	oct 21	density growth - growing bones
tue	oct 26	density growth - finite elements for growth
thu	oct 28	midterm
tue	nov 02	volume growth - growing tumors
thu	nov 04	volume growth - finite elements for growth / theory
tue	nov 09	volume growth - finite elements for growth / matlab
thu	nov 11	volume growth - growing arteries
tue	nov 16	volume growth - growing hearts
thu	nov 18	remodeling - remodeling arteries and tendons
tue	nov 30	class project - discussion, presentation, evaluation
thu	dec 02	class project - discussion, presentation, evaluation
thu	dec 02	written part of final projects due

introduction

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- 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

introduction

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The phenomenon of twisted growth: humeral torsion in dominant arms of high performance tennis players

R.E. Taylor^a, C. Zheng^a, R.P. Jackson^b, J.C. Doll^a, J.C. Chen^b, K.R.S. Holzbaur^c, T. Besier^d and E. Kuhl^{ab*}

^aDepartment of Mechanical Engineering, Stanford University, Stanford, CA, USA; ^bDepartment of Bioengineering, Stanford University, Stanford, CA, USA; ^cDepartment of Biomedical Engineering, Wake Forest University School of Medicine, Winston-Salem, NC, USA; ^dDepartment of Orthopaedic Surgery, Stanford University, Stanford, CA, USA

(Received 27 November 2007; final version received 2 May 2008)

This manuscript is driven by the need to understand the fundamental mechanisms that cause twisted bone growth and shoulder pain in high performance tennis players. Our ultimate goal is to predict bone mass density in the humerus through computational analysis. The underlying study spans a unique four level complete analysis consisting of a high-speed video analysis, a musculoskeletal analysis, a finite element based density growth analysis and an X-ray based bone mass density analysis. For high performance tennis players, critical loads are postulated to occur during the serve. From high-speed video analyses, the serve phases of maximum external shoulder rotation and ball impact are identified as most critical loading situations for the humerus. The corresponding posts from the video analysis are reproduced with a musculoskeletal analysis tool to determine muscle attachment points, muscle force vectors and overall forces of relevant muscle groups. Collective representative muscle forces of the deltoid, latissimus dorsi, pectoralis major and triceps are then applied as external loads in a fully 3D finite element analysis. A problem specific nonlinear finite element based density analysis tool is developed to predict functional adaptation over time. The density profiles in response to the identified critical muscle forces during serve are qualitatively compared to X-ray based bone mass density analyses.

Keywords: bone mass density changes; functional adaptation; musculoskeletal analysis; finite element analysis; sports medicine

student project - tennis player

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Modeling Bone Growth in High-Performance Tennis Players

Rebecca Taylor¹, Chunhua Zheng¹, Ryan Jackson¹, Joey Doll¹, Amir Shamloo¹, Ellen Kuhl¹
Stanford University¹, Stanford School of Medicine²

Purpose

It is well known that exercise-induced loads cause bone hypertrophy in the dominant arm of tennis players; this phenomenon has been documented by numerous studies of players who began play at pre-pubescent ages¹. However, the details that describe the processes of growth and remodeling that accompany this observation are unknown².

In addition, it is unclear as to which are the dominant variables that shape bone growth: muscular loading, impact forces during play or biological factors. We hypothesize that we can model this bone hypertrophy using a finite element growth model and that simulation gives further insight into the interplay between load and biological response.

Methods

Figure 2: Observation of serve posture suggests that humerus remains aligned with shoulders through serve. Humeral torsion is identified as most critical motion influencing bone growth in tennis players.

Figure 3: Critical serve posture at moment of racket-ball contact.

Figure 4: Meshed humerus in OpenSim (left) and finite element mesh (right) with 1182 nodes and 4362 linear tetrahedral elements; muscle forces approximated with OpenSim.

Results

The humerus was chosen for our study because it is the least complex of the arm bones. We investigated various loading scenarios and found tennis players to be excellent subjects because they show asymmetrical bone growth, and bone size in the non-dominant arm can be used as a control. We hypothesize that peak loading conditions occur during the high-speed serve. Based on video observation of tennis serves, we determined a posture for peak humerus stress. From this, approximate muscle forces were calculated with OpenSim. These forces were applied as external loads in a finite element growth model developed in class.

Figure 5: Density changes with increasing number of load cycles.

Conclusions

The encouraging results of our study could be of equal benefit to high performance athletes and patients with degenerative bone diseases. Based on patient-specific studies, optimized training strategies can be developed to promote bone growth.

References

- 1) Jones HH, Priest JD, Hayes WC, Taborer CA, Nagel DA. Humeral hypertrophy in response to exercise. *J Bone Joint Surg Am.* 1977;59:304-309.
- 2) Pearson CM, Lederman CE. The study of Wolff's "law": Ontology and responses to mechanical loading in cortical bone. *Yearbook Phys Anthr.* 2004;47:63-90.
- 3) Jacobs CR, Lavender MC, Besier DS, Fong JC, Carter DR. Numerical instabilities in bone remodeling simulations. *J Biomech.* 1995;28:449-459.

Acknowledgments

We would like to thank Thor Besier for sharing his images, video, and density study data with us. Many thanks to Scott Delp for granting us access to OpenSim and Kate Holzbaur for sharing her upper limb model with us and for graciously assisting us throughout our study.

http://biomechanics.stanford.edu/mechanics_of_growth <https://amtk.org/homeraingrowth>

Biomechan Model Mechanobiol (2007) 6:321–331
DOI 10.1007/s10237-006-0062-x

ORIGINAL PAPER

Computational modeling of arterial wall growth

Attempts towards patient-specific simulations based on computer tomography

E. Kuhl · R. Maas · G. Himpel · A. Menzel

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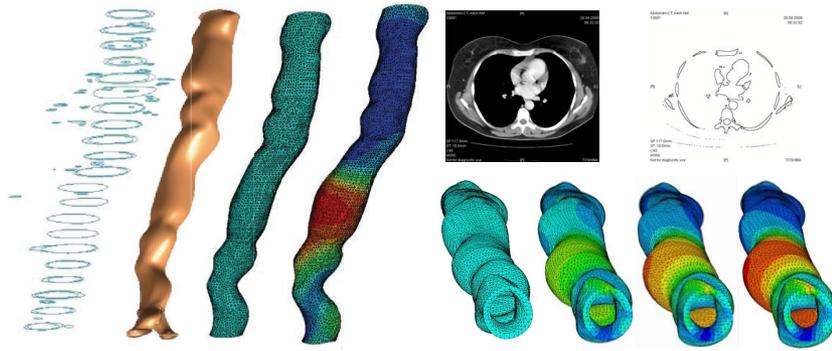
Abstract The present manuscript documents our first experiences with a computational model for stress-induced arterial wall growth and in-stent restenosis related to atherosclerosis. The underlying theoretical framework is provided by the kinematics of finite growth combined with open system thermodynamics. The computational simulation is embedded in a finite element approach in which growth is essentially captured by a single scalar-valued growth factor introduced as internal variable on the integration point level. The conceptual simplicity of the model enables its straightforward implementation into standard commercial finite element codes. Qualitative studies of stress-induced changes of the arterial wall thickness in response to balloon angioplasty or stenting are presented to illustrate the features of the suggested growth model. First attempts towards a patient-specific simulation based on realistic artery morphologies generated from computer tomography data are discussed.

student project - arterial wall growth

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patient specific virtual stent implantation



from ct to finite element model

student project - arterial wall growth

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ON SIMULATING GROWTH AND FORM

FOR BETTER OR FOR WORSE, and on many levels, our tissues never stop growing and changing. While developing from childhood to old age, we grow not only bone, cartilage, fat, muscle and skin, but also toughened arteries, scars for our wounds, and, sometimes, deadly tumors.

"Computation is a great tool to study growth," says Ellen Kuhl, PhD, assistant professor of mechanical engineering and bioengineering at Stanford University, "because it lets us understand all those fascinating biological processes we can't otherwise see and predict."

A simulated aorta, based on computer tomography data from a specific patient, highlights the effects of stent surgery (shown before surgery as well as 4 days, 16 days, and 23 days after surgery). Cyan shading shows artery walls with normal thickness; blue shading shows thinning walls; red shading shows thickened walls. In a real patient, the tissue growth shown in red would have resulted in in-stent restenosis. Courtesy of Ellen Kuhl. Reprinted

www.biomedicalcomputationreview.org

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Computational modeling of hip replacement surgery: Total hip replacement vs. hip resurfacing

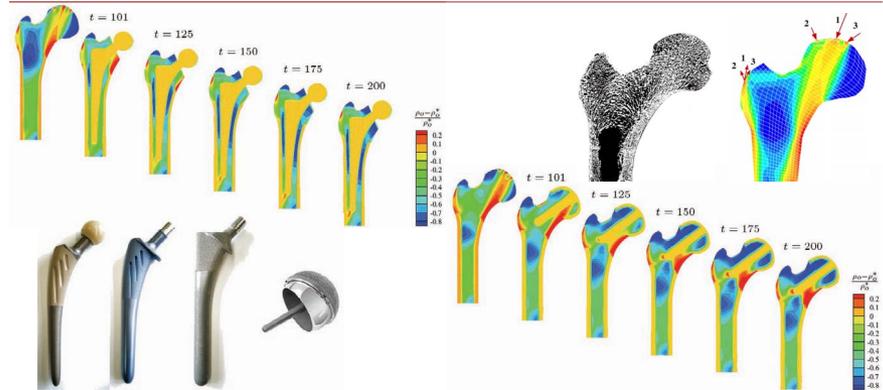
E. Kuhl & F. Balle

The motivation of the present work is the computational simulation of hip replacement surgery by means of a finite element approach based on open system thermodynamics. Its key feature is a non-constant material density, which is allowed to adapt with respect to changes in the mechanical loading environment. From a computational point of view, the density is treated as an internal variable. Its evolution is governed by a first order rate equation, the balance of mass, which is enhanced by an additional mass production term to account for growth. An implicit Euler backward scheme is suggested for its time discretization. The algorithmic determination of the material density based on a local Newton iteration is presented. To ensure quadratic convergence of the global Newton Raphson solution scheme, a consistent linearization of the discrete algorithmic equations is carried out. Finally, two alternative medical techniques in hip arthritis are compared, the conventional total hip replacement strategy and the more recent hip resurfacing technology. The result of the suggested remodeling algorithm is shown to agree remarkably well with clinically observed phenomena.

student project - hip replacement

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how do bones grow?



conventional hip replacement vs hip resurfacing

student project - hip replacement

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Computational modeling of growth

Systemic and pulmonary hypertension in the heart

M.K. Rausch · A. Dam · S. Göktepe · O.J. Abilez · E. Kuhl

Received: date / Revised version: date

Abstract We introduce a novel constitutive model for growing soft biological tissue and study its performance in two characteristic cases of mechanically-induced wall thickening of the heart. We adopt the concept of an incompatible growth configuration introducing the multiplicative decomposition of the deformation gradient into an elastic and a growth part. The key feature of the model is the definition of the evolution equation for the growth tensor which we motivate by pressure-overload induced sarcomerogenesis. In response to the deposition of sarcomere units on the molecular level, the individual heart muscle cells increase in diameter, and the wall

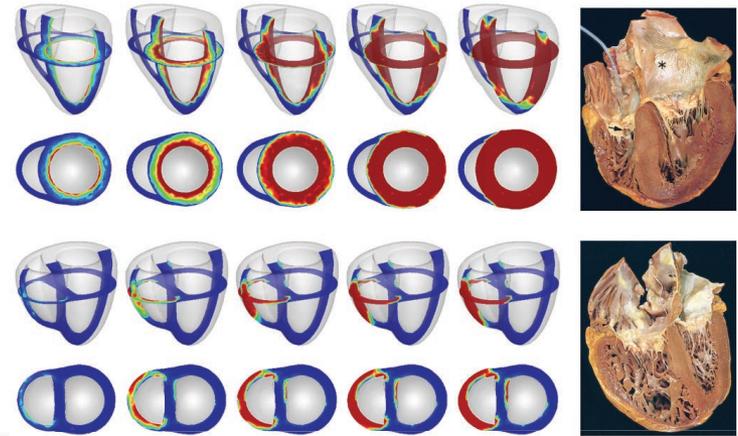
of the heart becomes progressively thicker. We present the underlying constitutive equations and their algorithmic implementation within an implicit nonlinear finite element framework. To demonstrate the features of the proposed approach, we study two classical growth phenomena in the heart: left and right ventricular wall thickening in response to systemic and pulmonary hypertension.

Keywords Biomechanics; growth; remodeling; finite elements; hypertension; hypertrophy

student project - hypertension

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why does the heart wall get thicker?



student project - hypertension

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what's growing?

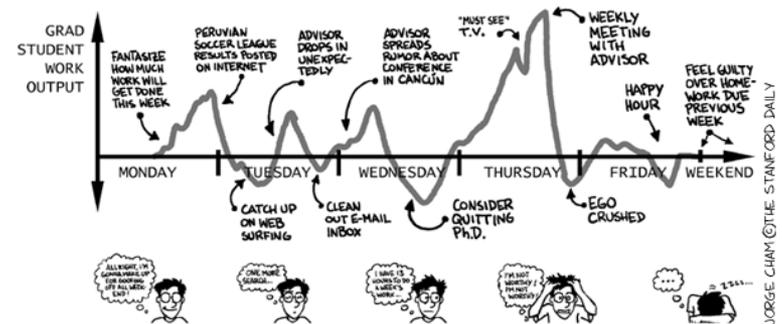


classical engineering materials are not!

introduction

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what's growing?



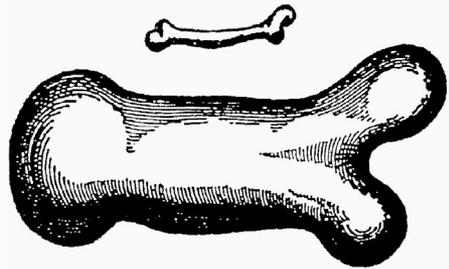
grad student work output

J. Cham "Piled higher and deeper", [1999]

introduction

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history - 17th century



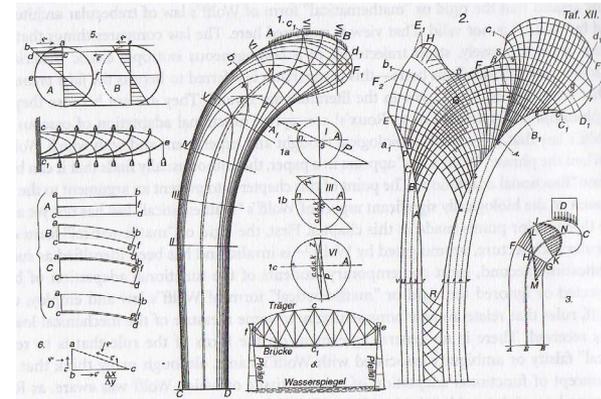
„...dal che e manifesto, che chi volesse mantener in un vastissimo gigante le proporzioni, che hanno le membra in un uomo ordinario, bisognerebbe o trouar materia molto piu dura, e resistente per formame l'ossa o vero ammettere, che la robustezza sua fusse a proporzione assai piu fiacca, che negli huomini de statura mediocre; altrimenti crescendogli a smisurata altezza si vedrebbero dal proprio peso opprimere, e cadere...“

Galleo, "Discorsi e dimostrazioni matematiche", [1638]

introduction

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history - 19th century

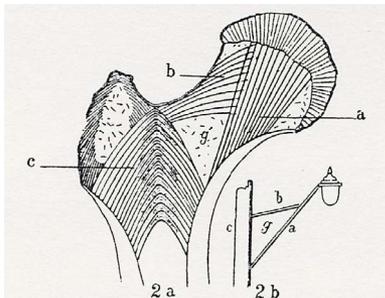


Culmann & von Meyer „Graphic statics“ [1867]

introduction

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history - 19th century



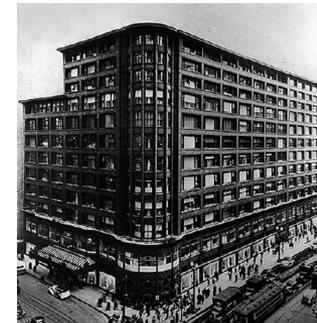
„...es ist demnach unter dem gesetze der transformation der knochen dasjenige gesetze zu verstehen, nach welchem im gefolge primaerer abaenderungen der form und inanspruchnahme bestimmte umwandlungen der inneren architectur und umwandlungen der aeusseren form sich vollziehen...“

Wolff „Gesetz der Transformation der Knochen“ [1892]

introduction

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history - 19th century



carson pirie scott store
Sullivan [1904]

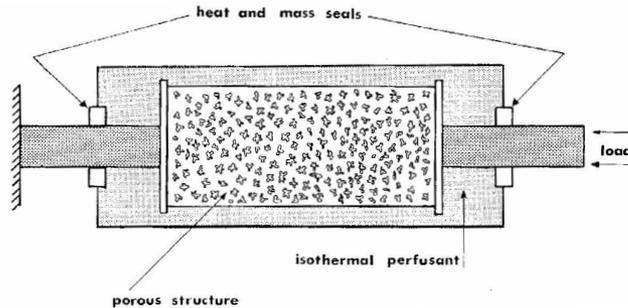
„...whether it be the sweeping eagle in his flight or the open apple-blossom, the tolling work-horse, the blithe swan, the branching oak, the winding stream at its base, the drifting clouds, over all the coursing sun, form ever follows function, and this is the law...“

Sullivan „Form follows function“ [1896]

introduction

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history - 20th century



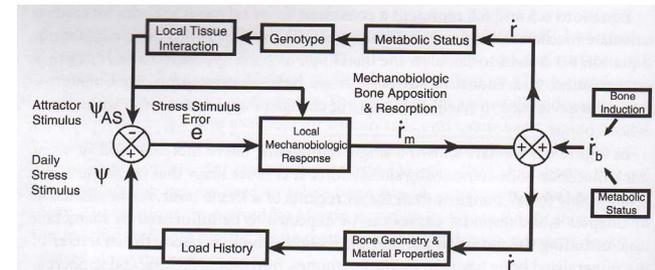
„...the system consisting of only the porous structure without its entrained perfusant is open with respect to momentum transfer as well as mass, energy, and entropy transfer. we shall write balance and constitutive equations for only the bone...“

Cowin & Hegedus „Theory of adaptive elasticity“ [1976]

introduction

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history - 20th century



„...the relationship between physical forces and the morphology of living things has piqued the curiosity of every artist, scientist, or philosopher who has contemplated a tree or drawn the human figure. its importance was a concern of galileo and later thompson whose writings remind us that physical causation plays an inescapable role in the development of biological form...“

Beaupré, Carter & Orr „Theory of bone modeling & remodeling“ [1990]

introduction

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history - 20th century



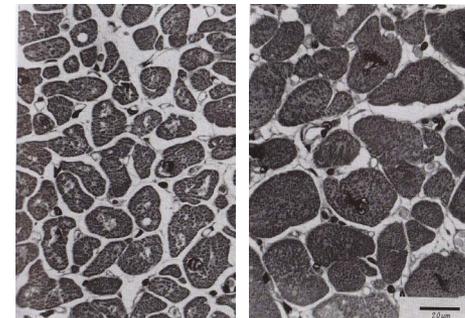
„hypertrophy of the heart: comparison of cross sections of a normal heart (bottom), a heart chronically overloaded by an unusually large blood volume (left) and a heart chronically overloaded by an unusually large diastolic and systolic left ventricular pressure (right)“

Fung „Biomechanics - Motion, flow, stress, and growth“ [1990]

introduction

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history - 20th century



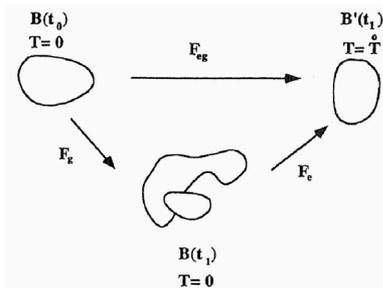
„hypertrophy of the heart: histology of a normal heart (left) and pressure overloaded heart (right) photographed at the same magnification - muscles in the hypertrophic heart (right) are much bigger in diameter than those of the normal heart (left).“

Fung „Biomechanics - Motion, flow, stress, and growth“ [1990]

introduction

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history - 21th century



Rodriguez, Holger & McCulloch [1994]

„...the process of growth can be seen as an evolution of material point neighbourhoods in a fixed reference configuration. the growth process will cause the development of material inhomogeneities responsible for residual stresses in the body...“

Epstein & Maugin „Theory of volumetric growth“ [2000]

introduction

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growth, remodeling and morphogenesis

growth [grouθ] which is defined as added mass, can occur through cell division (hyperplasia), cell enlargement (hypertrophy), secretion of extracellular matrix, or accretion @ external or internal surfaces. negative growth (atrophy) can occur through cell death, cell shrinkage, or resorption. in most cases, hyperplasia and hypertrophy are mutually exclusive processes. depending on the age of the organism and the type of tissue, one of these two growth processes dominates.

Taber „Biomechanics of growth, remodeling and morphogenesis“ [1995]

introduction

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growth, remodeling and morphogenesis

remodeling [ri'mad.l.ɪŋ] involves changes in material properties. These changes, which often are adaptive, may be brought about by alterations in modulus, internal structure, strength, or density. for example, bones, and heart muscle may change their internal structures through reorientation of trabeculae and muscle fibers, respectively.

Taber „Biomechanics of growth, remodeling and morphogenesis“ [1995]

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growth, remodeling and morphogenesis

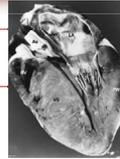
morphogenesis [mɔːr.fɒ'dʒen.ə.sɪs] is the generation of animal form. usually, the term refers to embryonic development, but wound healing and organ regeneration are also morphogenetic events. morphogenesis contains a complex series of stages, each of which depends on the previous stage. during these stages, genetic and environmental factors guide the spatial-temporal motions and differentiation (specification) of cells. a flaw in any one stage may lead to structural defects.

Taber „Biomechanics of growth, remodeling and morphogenesis“ [1995]

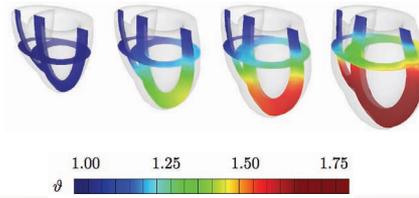
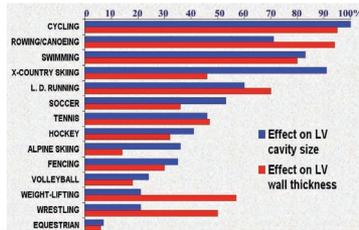
introduction

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athlete's heart - a patient-specific simulation



- growth beyond normal size due to **significant exercise**
- training-induced changes are typically **reversible**
- adaptation driven by **elevated pressure** and **increased filling**
- cardiac **output increases from 6 l/min at rest up to 40 l/min**
- cardiac **mass increases up to 50%**



how do skeletal muscles grow when we train?

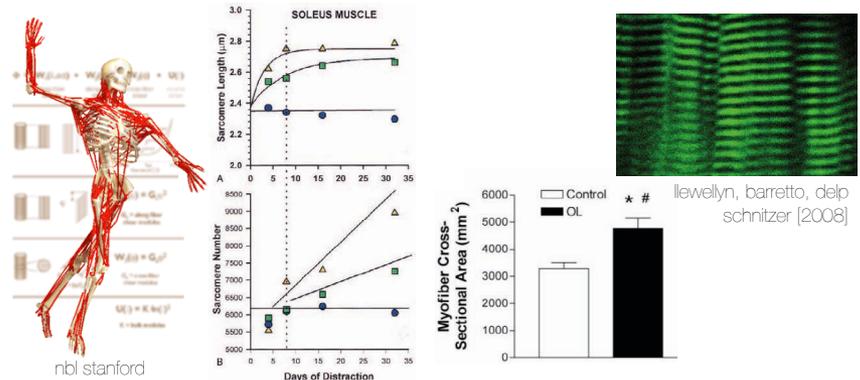


Figure. Response of rat soleus muscle to overstretch (left). Sarcomere length (top) and sarcomere number (bottom). During the initial phase of loading, days 4 and 8, sarcomere length progressively increases. Beyond this point, however, sarcomere length remains constant and there is a progressive increase of the number of sarcomeres in series. Response of rodent skeletal muscle to overload (right). Myofiber cross section area increases with increased loading.

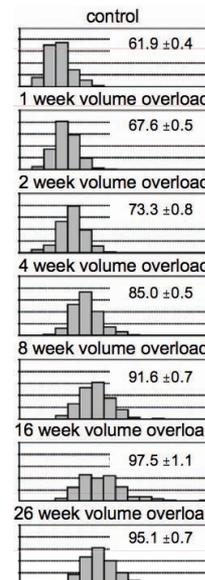
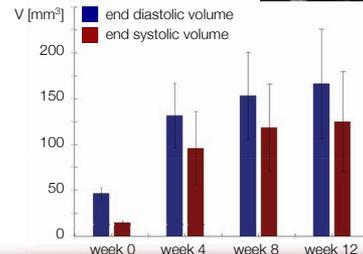
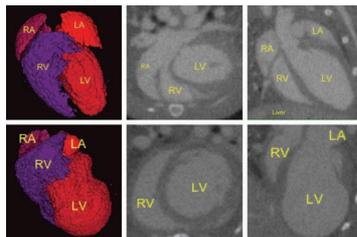
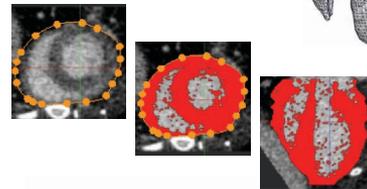
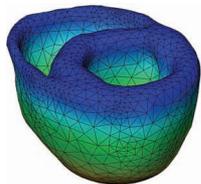
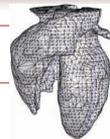
group project - athlete's heart

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group project - getting stronger

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heart attack! how does the heart grow?



how do cells grow?



- how do cardiomyocytes change their length?
- left ventricle **enlarged 4-28%** and **dilated 14% at week one** after volume overload
- LV dilation by **cardiomyocyte elongation**
- myocyte elongation by **serial sarcomere deposition**
- sarcomere **number increases linearly** from 62 to 85
- sarcomere deposition **rate is linear in weeks 1 to 4** & decays smoothly from week 4 to saturation at 26

a literature study / review paper

group project - mouse heart

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group project - sarcomerogenesis

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