01 - motivation - everything grows!

... what we do ...

- kinematic equations for finite growth
  \[ F = F_e \cdot F_g \]
- balance equations for open systems
  \[ D_t \rho_0 = \text{Div}(\mathbf{R}) + \mathbf{R}_0 \]
  \[ \rho_0 D_v \mathbf{v} = \text{Div}(\mathbf{P}) + \mathbf{b}_0 \]
- constitutive equations for living tissues
  \[ \mathbf{P} = \mathbf{P}(\rho_0, F, F_g) \]
- fe analyses for biological structures

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

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  \[ F = F_e \cdot F_g \]
- balance equations for open systems
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- constitutive equations for living tissues
  \[ \mathbf{P} = \mathbf{P}(\rho_0, F, F_g) \]
- fe analyses for biological structures

... because biological structures are ...

... what we do ...

continuum- & computational biomechanics
balance equations for open systems
\[ D_t \rho_0 = \text{Div}(R) + \mathcal{R}_0 \]
\[ \rho_0 D_t v = \text{Div}(P) + b_0 \]
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... what we do ...
... why we do what we do ...

kinematic equations for finite growth
\[ F = F_e \cdot F_g \]

balance equations for open systems
\[ D_t \rho = \nabla \cdot (\gamma + R) \]

constitutive equations
\[ P = P(\sigma, \varepsilon) \]

fe analyses for biological structures

... because biological structures are ...

living
highly deformable
anisotropic
nonlinear
inelastic
inhomogeneous

... what we do ...

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

kinematic equations for finite growth
\[ F = F_e \cdot F_g \]

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... what we do ...

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 problem-specific 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

me337 - syllabus 2007

<table>
<thead>
<tr>
<th>Day</th>
<th>Date</th>
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<tbody>
<tr>
<td>Tue</td>
<td>Sep 21</td>
<td>motivation - everything grows</td>
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<tr>
<td>Thu</td>
<td>Sep 23</td>
<td>basics and maths - notation and tensors</td>
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<td>Sep 28</td>
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<td>volume growth - growing hearts</td>
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<td>Thu</td>
<td>Nov 18</td>
<td>remodeling - remodeling arteries and tendons</td>
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<td>Thu</td>
<td>Dec  2</td>
<td>class project - discussion, presentation, evaluation</td>
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<tr>
<td>Thu</td>
<td>Dec  2</td>
<td>written part of final projects due</td>
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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.
Computational modeling of arterial wall growth

Attempts towards patient-specific simulations based on computer tomography

E. Kuhl - R. Maas - G. Hinze - A. Menzel

Abstract: The present manuscript documents our first experiences with a computational model for stress-induced arterial wall growth and its transfer to realistic patient-specific geometries. The underlying theoretical framework is represented 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 an 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.

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."

patient specific virtual stent implantation

from ct to finite element model

student project 2006 - arterial wall growth

student project 2007 - tennis player
The phenomenon of twisted growth: humeral torsion in dominant arms of high performance tennis players


Department of Emergency Medicine, Stanford University, Stanford, CA, USA; *Department of Biomedical Engineering, Wake Forest University School of Medicine, Winston-Salem, NC, USA; **Department 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 level of 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 pose from these video analyses 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 to a fully 3D finite element analysis. A problem specific non-linear 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

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Computational modeling of growth
Systemic and pulmonary hypertension in the heart

M.K. Rasouli, A. Donat, S. Gillis, O.J. Alldrin, K. Kuhl

Research date / First draft date: June 2010

Abstract: We introduce a novel constitutive model for growing soft biological tissues and study its performance in two characteristic cases of mechanically induced wall thinning of the heart. We adopt the concept of an implicit constitutive framework introducing the multiplicative decomposition of the deformation gradient tensor into a growth and a growth part. The key features of the model is the definition of the evolution equation for the growth tensor, which we motivate by pressure-induced wall stiffness. In response to the deposition of collagenous units at the intercellular level, the interstitial 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, stress-rate constitutive framework. To demonstrate the features of the proposed approach, we study two classical growth and hypertrophy problems in the heart: left and right ventricular wall thinning in response to systemic and pulmonary hypertension.

Keywords: Computational models, remodeling, finite element, hypertrophy, remodeling.

References:


Acknowledgments:
We wish to thank the NIH for their support of this work through grants from National Institutes of Health.
Computational modeling of bone density profiles in response to gait: A subject-specific approach

Henry Pang¹, Abhishek P. Shiwalkar¹, Chris M. Madormo¹, Rosecca E. Taylor¹, Thomas P. Andricacci¹, Ellen Kuhl⁴

class project me357
mechanics of growth

<table>
<thead>
<tr>
<th>trial</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>mean</th>
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<td>max knee force [% BW]</td>
<td>94.9</td>
<td>94.4</td>
<td>90.4</td>
<td>96.2</td>
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how does henry’s bone grow?


Growing skin: A computational model for skin expansion in reconstructive surgery

Adrián Buganza Tepete³, Christopher Joseph Ploch¹, Jonathan Wong⁴, Arun K. Gosain⁵, Ellen Kuhl⁴

student project 2010 – skin growth

how does skin grow?
Stretching Skeletal Muscle: Chronic Muscle Lengthening through Sarcomerogenesis

Alexander M. Zöllner, Oscar J. Abilés, Markus Bül, Ellen Kuhl

Department of Mechanical Engineering, Stanford University, Stanford, California, United States of America; J. Abilés, M. Bül, E. Kuhl, Department of Biomedical Engineering, Stanford University, Stanford, California, United States of America; A. Zöllner, Department of Surgery, Stanford University, Stanford, California, United States of America

Abstract

Skeletal muscle responds to passive overstretch through sarcomerogenesis, the creation and serial deposition of new sarcomere units. Sarcomerogenesis is critical to muscle function: it gradually repositions the muscle back into its optimal operating regime. Animal models of immobilization, limb lengthening, and tendon transfer have provided significant insight into muscle adaptation in vivo. Yet, to date, there is no mathematical model that allows us to predict how skeletal muscle adapts to mechanical stress in situ. Here we propose a novel mechanical model for chronic longitudinal muscle growth in response to passive mechanical stretch. We characterize growth through a single scalar-valued internal variable, the sarcomere number. Sarcomerogenesis, the evolution of this variable, is driven by the elastic mechanical stretch. To analyze realistic, three-dimensional muscle geometries, we embed our model into a nonlinear finite element framework. In a chronic limb lengthening study with a muscle stretch of 1.14, the model predicts an acute sarcomere lengthening from 3.09 mm to 3.31 mm, and a slower, gradual return to the initial sarcomere length within two weeks. Compared to the experiment, the acute model error was 0.59%, while the chronic model error was 2.13%, which lies within the range of the experimental standard deviation. Our model explains, from a mechanical point of view, why gradual multi-step muscle lengthening is less invasive than single-step lengthening. It also explains regional variations in sarcomere length, wherein closer and longer-from-the-muscle-tendon interface. Once calibrated with a richer data set, our model may help surgeons to prevent muscle overstretch and make informed decisions about optimal stretch increments, stretch timing, and stretch amplitudes. We anticipate our study to open new avenues in orthopedic and reconstructive surgery and enhance treatment for patients with failed tendon transfers, tendon transfers, tendon tears, and chronically stretched muscles.

Introduction

What’s growing?

Classical engineering materials are not!

Grad Student Work Output

J. Cham “Piled higher and deeper” [1999]
...dal che e manifesto, che chi volesse mantener in un vastissimo gigante le proporzioni, che hanno le membra in un huomo ordinario, bisognerebbe o trouar materia molto più dura, e resistente per formarne l'ossa o vero ammettere, che la robustezza sua fusse a proporzione assai più lieve, che negli huomini de statu medio; altimmente crescendogli a smisurata altezze si vedrebbono dal proprio peso opprimere, e cadere..."  
Galileo, "Discorsi e dimostrazioni matematiche" [1638]

...es ist demnach unter dem gesetze der transformation der knochen dasjenige gesetz zu verstehen, nach welchem im gefolge primaer abanderungen der form und inanspruchnahme bestimmte umwandlungen der inneren architectur und umwandlungen der aeusseren form sich vollziehen..."  
Wolff „Gesetz der Transformation der Knochen“ [1892]

...whether it be the sweeping eagle in his flight or the open apple-blossom, the toiling 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]
...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]

...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]

 „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]

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

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

growth, remodeling and morphogenesis

**growth** 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]

**remodeling** 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]

**morphogenesis** 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]
**Possible final project – airway wall remodeling**

- Siggs, Hrous, Drazen, Kamm [1997], Zhang, Zhao, Suo, Jiang [2009], Jin, Cai, Suo [2011], Moulton, Goriely [2011], Li, Cao, Feng, Gao [2011], Cao, Li, Feng [2012], Papastavrou, Steinmann, Kuhl [2013]

**Possible final project – brain folding**

- Xu, Knudsen, Akiran, Kroeker Berry, Taber [2010]

---

**Asthma – how does the airway wall grow?**

- 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%

**Brain developments – how do brain folds grow?**

- **Left ventricle enlarged** 4-28% and **dilated 14%**
- **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

---

**Athlete’s heart - a patient-specific simulation**

- How do cardiomyocytes change their length?
- Left ventricle enlarged 4-28% and dilated 14%
- 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

---

**Possible final project – athlete’s heart**

- A literature study / review paper

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**Possible final project - sarcomerogenesis**

- A literature study / review paper
how does skeletal muscle grow when we work out?

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.

possible final project - growing stronger

high heels – how do your muscles shorten?

possible final project – high heels