Joakim Sundnes[*], Andrew D. McCulloch[†]

Computational heart mechanics

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[*] Simula Research Laboratory and Department of Informatics, University of Oslo.
[†] Bioengineering Department, University of California, San Diego.

Preface

The purpose of this book is to introduce students and researchers to the principles of computational soft tissue mechanics, and provide them with the necessary background to use, understand and potentially build computational software for heart mechanics. A brief general introduction to nonlinear solid mechanics is given, but the reader is referred to other books for a more detailed explanation of these topics. Obtaining one of these books is highly recommended, since the present tex is compact and may be difficult to read without any background in continuum mechanics. The book will include a number of relevant examples that give the reader both an idea of what the models can be used for, and a collection of âĂIJrecipesâĂİ for using and solving the models.

From the doconce book setup:

1. Chapters can exist as stand-alone documents in different formats:
   - traditional LaTeX-style PDF report,
   - web pages with various fancy stylings (e.g., Sphinx, Bootstrap) and possibility for multi-media elements,
   - IPython notebooks,
   - blog posts (not exemplified here, but straightforward[1]),
   - wiki (if you do not need mathematical typesetting).
2. Chapters can be flexibly assembled into a traditional LaTeX-based PDF book for a traditional publisher, or a fancy ebook.
3. The book and the individual chapter documents may have different layouts.
4. Active use of preprocessors (Preprocess and Mako) makes it easy to have different versions of the chapters, e.g., a specialized version for a course and a general version for the world book market).

[1] `http://hplgit.github.io/doconce/doc/pub/manual/html/manual.html#blog-posts`

5. DocOnce has support for important elements in teaching material: eye-catching boxes (admonitions), quizzes, interactive code, videos, structured exercises, quotes.
6. Study guides or slides can easily be developed from the running text and stored along with the chapters. These can be published as LaTeX Beamer slides, reveal.js slides, and IPython notebooks.

These features have the great advantage that a book can evolve from small documents, thereby making the barrier for book writing much smaller. Also, several appealing ebook formats can be produced, both for the book and the individual chapter documents. The chances that your students read a chapter on the bus becomes larger if the chapter is available as attractive, screen-fit Bootstrap pages on the smart phone than if you just offer the classic LaTeX PDF which actually requires a big screen or a printer.

Implementation of point 1 and 2 is not trivial and requires some rules that might not feel natural at first sight in the setup. Writing a book soon becomes a technically and mentally complex task, just like developing a software system. For the latter people have invented a lot of sophisticated technologies and best practices to deal with the complexity. The present setup for books is a similar collection of my own technologies and best practices, developed from writing thousands of pages. In particular, the setup has been successfully used for the large-scale 900-page Springer book "A Primer on Scientific Programming with Python" [2] (individual chapters of this book, e.g. [1], can be examined online in various ebook formats) as well as for books in the works[2].

To use this setup, just clone the repository[3] and you have the directory structure, the scripts, and example files to get started with a book project at once! The source files for this book (especially in `doc/src/chapters/rules`) constitute nice demonstrations for learning about basic and advanced DocOnce writing techniques.

April 2015 *Hans Petter Langtangen*

[2] `http://hplgit.github.io/num-methods-for-PDEs/doc/pub/index.html`

[3] `https://github.com/hplgit/setup4book-doconce`

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Chapter 1
Introduction and Motivation

Chapter 2
Introduction and motivation (appr. 10-15 pages)

2.1 Structure of the heart and cardiac muscle

2.1.1 Heart anatomy and mechanical function

Overview of heart anatomy and structure, focusing on the mechanical function

2.1.2 Structure of cardiac muscle tissue

Outline of muscle tissue organization;

- Overview of tissue structure
- Overview of cardiomyocyte structure, introducing the contractile proteins
- The extracellular matrix

2.2 The mechanics of heart contraction

Brief overview of the pumping function of the heart viewed as a mechanical multi-scale problem. A top-down view may be most illustrative, linking the different phases of the heart cycle (PV-loop, Wiggers diagram) to the mechanics of the tissue, the myocyte, and the sub-cellular structures.

2.3 Computational mechanics challenges

From a viewpoint of computational mechanics, outline the most important challenges of modeling heart mechanics.

2.3.1 Computational challenges of multiscale problems

Referring to the outline of heart mechanics as a multiscale problem in Section 2.2, outline current modeling paradigm and the general computational challenges related to solving multiscale, multiphysics problems.

2.3.2 Mechanics of soft tissues

Outline classical aspects known to be challenging in continuum mechanics, and describe how they are present in models of passive muscle tissue:

- large deformations
- Non-linear material behavior
- Incompressibility and related numerical problems
- High anisotropy
- Uncertainty and variability in material parameters

2.4 Heart disease and mechanical dysfunction

Some re-organization is possible here, maybe placing this part before the outline of the mechanical problem.

- Brief summary of heart disease in general
- Outline selected heart problems where mechanical dysfunction of the heart muscle is an important factor. Of course, the distinction is not entire clear, but this would exclude severe arrhytmia and direct effects of valve dysfunction, but include heart failure and remodeling driven by load imbalance caused by electrical dyssynchrony or valve problems.

2.5 Outline and scope of the book

Should possibly (probably) be moved to a preface. Outline the book's content, focus and intended audience, and, most importantly, list the many important topics that will not be covered by the book.

Chapter 3

Introduction to Non-Linear Solid Mechanics

Chapter 4

Introduction to non-linear solid mechanics (appr. 40 p)

A compact introduction to the necessary theory. Start the chapter with a brief ouline of its purpose, that we want to employ the laws of Newton to arrive at dynamic and static balance laws governing the relation between forces and deformation. Ths brief introduction will motivate the concepts of strain and stress to be introduced through the chapter.

4.1 Kinematics

Introduce the necessary framework for describing movement and deformation of soft tissues:

- Introduce the displacement field and mapping between the reference and undeformed configuration, also briefly mentioning the generalization to intermediate configurations as used in growth models and active strain models of contraction. Introduce the deformation gradient.
- Describe the distinction between Lagrangian and Eulerian description of field quantities.

4.2 The concept of strain

- Describe the purpose of and general requirements to deformation measures, i.e. the need for a precise measure of local deformations, excluding rigid body motion. Explain why neither the displacement field nor the deformation gradient are suitable measures of deformation.
- Introduce the most widely used deformation and strain tensors, including the linear strain tensor (for familiarity), the Green-Lagrange strain tensor,

the left Cauchy-Green tensor. Possibly a couple more, but most likely just list these and cite other sources for details.
- Describe the concept of frame invariance, and introduce the primary strain invariants.

4.3 The concept of stress

- Basic intriduction to the stress vector and (Cauchy) stress tensor
- Explain the problems of using the Cauchy stress in large deformation mechanics
- Introduce the most commonly used stress tensors in soft tissue mechanics, i.e. the first and second Piola-Kirckhoff stress tensors.
- List alternative, potentially relevant stress tensors, cite other sources for details.

4.4 Balance equations

Present a compact derivation of the fundamental laws of motion, based on conservation of linear momentum.

- Euler description, Cauchy stress
- Lagrange description, Piola-Kirchoff stress
- Discuss the relative significance of the terms, motivate the quasi-static approach and the neglection of body forces
- Discuss the general nature of the equation, and relate this to the mismatch between number of equations and unknowns. This motivates the need for constitutive models.

4.5 Modeling material behavior

Give a general introduction to constitutive modeling, explicitly neglecting the complex behavior of the heart muscle and other soft tissues. For completeness and to increase the understanding of the balance equations presented above, describe the general behavior of fluids and solids, briefly list models for “advanced” solids (visco-elasticity, plasticity etc), and proceed to describe simpler elastic and hyperelastic models. This section has two purposes; (1) to give a soft introduction to material modeling before diving into the more complex and realistic case, and (2) to arrive at some fairly compact model problems that will be used to introduce the computational techniques in the next chapter.

Chapter 5
Computational techniques for elasticity

Chapter 6

Computational techniques for elasticity (20-30 p)

It may be discussed where this chapter is to be put, but most likely it is useful to introduce the solution methods before introducing the more complex constitutive laws. This may give a fairly compact description, and since the methods have already been introduced, the necessary extensions and modifications may be described in subsequent chapters.

6.1 Numerical methods for PDEs

Brief, general discussion of numerical methods for PDE problems, referencing the known challenges outlined earlier. Introduce the finite element method as the method of choice for spatial discretization of the mechanics problem.

6.2 Outline of the finite element method

Brief introduction to the finite element method for PDEs, using the standard Poisson problem as model equation.

6.3 FEM for linear and non-linear elasticity

- FEM for linear elasticity (Navier's equation)
- FEM for non-linear hyperelasticity, derived in the standard form, but with notes on equivalent concepts such as the principle of virtual work and principle of stationary potential energy.

- Linearization techniquez for FE equations arising from non-linear hyperelasticity
- Element choices, incompressibility and locking

Chapter 7
Constitutive laws for passive heart tissue

Chapter 8

Constitutive laws for passive heart tissue (20-30 p)

To limit the scope, and keep the focus on commonly used models, the focus should probably be on hyper-elasticity. Still, some justification of why we disregard visco-elastic effects should probably be included.

8.1 Modeling soft tissues

- Brief description of the exponential stress-strain behavior characteristic of soft tissues
- Simple constitutive laws based on strain components and strain invariants

8.2 Cardiac microstructure and anisotropy

(Possibly split this section in two, one covering standard anisotropic continuum models, and one focusing on the microstructure and related models.)

- Recapture and expand the description of cardiac microstructure from Chapter 2.1.2, and how this affects cardiac mechanical properties.
- Describe the necessary expansions of the models above to describe orthotropic and transversely isotropic material behavior, including examples of constitutive laws based on strain components and strain (pseudo-)invariants.
- Introduce the idea of a local (fiber) coordinate system, and how this enters the strain component based constitutive laws.
- Similar notes on spatially varying material directions for invariant-based models.

- Referring back to the first item above, introduce models that explicitly describe the cardiac microstructure, and discuss the fundamental differences from the continuum models.

8.3 Fitting material parameters

The purpose of this section is to give the readers a very brief introduction to how experiments are used to select the material parameters, and in particular to illustrate the difficulty and uncertainty associated with this part of the modeling.

- Brief review of experimental techniques to characterize passive material response, i.e. uniaxial and biaxial tests, shear tests etc. Not intended to be a complete presentation or discussion of experimental techniques, but discuss the different setups with respect to their ability to characterize anisotropic behavior.
- Brief review of material parameters encountered in the litterature, to illustrate variability
- Promises and limitations of image based techniques, for patient specific parameter fitting.

8.4 Computational techniques for passive muscle tissue

Present the necessary extensions of the solution methods from Chapter 6, in order to solve the equations of anisotropic hyeprelastic models with spatially varying material directions.

Chapter 9
Modeling cell and tissue contraction

Chapter 10
Modeling cell and tissue contraction (30 p)

In terms of limiting the scope, this may be the most difficult chapter. Clearly, covering all aspects of cell mechano-biology is not possible. My first thoughts are to ignore all electrophysiology, and carefully outline the scope and limitations at the start of the chapter. Then something like this:

10.1 Cardiomyocyte force development

- Expand on the general introduction given in Chapter 2 , to give a more detailed desription of how myocytes develop force.
- Describe important features that should be captured by a realistic model, including the cooperativity of the force-Ca relation, and the force-length and force-velocity relations. Focus on biophysical details and modelign issues, and briefly mention computational and numerical difficulties arising from these aspects.
- Present a model for force-development based on a cross bridge distortion model, in a relatively simple form, and illustrate how the model captures the features listed above.
- Possibly include a phenomenological model, i.e. based on the ideas introduced by the HMT model, as a model of substantially simplified computational complexity.

10.2 Cell to tissue coupling

- Describe coupling of single cell contraction to tissue mechanics, in terms of the standard active stress approach

- Possibly mention the active strain and hybrid approaches as alternatives to the standard form.
- Comment on computational and biophysical aspects of the two approaches

10.3 Computational models of active mechanics

- Expand the computational models introduced in Chapter 8, to include the actively contracting muscle.
- Illustrate the challenges of strongly coupled simulations, and discuss suitable computational techniques.

Chapter 11
Boundary conditions and whole heart models

Chapter 12
Boundary conditions and whole heart models (20-30 p)

In the interest of saving space, this should probably not cover whole heart models, but rather a simplified LV model. This choice will allow the description of most of the general features and challenges of whole heart models, without including too much detail. Possible contents will include:

12.1 The cardiac cycle revisited

- Recapture the phases of the cardiac cycle introduced in Chapter 2, and describe how these are connected to valvular events and the mechanics of the circulatory system.
- Introduce the concept of ventricular BCs by considering passive filling with a prescribed pressure

12.2 Models for the circulatory system

- Introduce a simple closed loop model for the hemodynamic boundary conditions,
- Comment on limitations and possible extensions of the simple model, but refer to other sources for actual models

12.3 Computational models of the beating heart

- Comment on implications for solution methods, and present extensions of previously derived methods to describe the full dynamic problem

- Examples of interesting simulation cases
- Possible discussion of limitations and possible extensions
- Biventricular models, either discussed as a possible extension or included in the form of a simple example

Chapter 13
Open problems in cardiac mechanics

Chapter 14
Open problems in cardiac mechanics

Describe open problems and unsolved challenges in cardiac mechanics modeling. This is still fairly open, but possible candidate sections include:

- The clinical perspective. What are the unsolved clinical challenges where (improved) mechanics models are promising tools?
- Understanding myocyte contraction, and the multiscale aspects of this process. While the microscopic scale of cell contraction may be well understood, there are unresolved questions in how the microscopic behavior can be properly incorporated into organ-scale models.
- Variability of material properties. Even for passive mechanics, the variability in reported material properties and parameters does not inspire confidence in model predictions. Should be discussed in view of the current modeling paradigm and the in vitro and in vivo techniques used for parameter fitting.

Remark. Documents that contain raw Mako code in verbatim code blocks cannot also be processed by Mako, and this is the case with the `mako` chapter. Since we need Mako for processing the rest of this book document, we are forced to compile the `mako` chapter as a stand-alone document (with the `--no_mako` option) and let this appendix be just a link to the this stand-alone document[1].

[1] `http://hplgit.github.io/setup4book-doconce/doc/pub/mako/pdf/main_mako.pdf`

References

[1] H. P. Langtangen. Loops and lists. *http://hplgit.github.io/primer.html/doc/pub/looplist*.

[2] H. P. Langtangen. *A Primer on Scientific Programming With Python*. Texts in Computational Science and Engineering. Springer, fourth edition, 2014.