

Preface

This book contains a collection of papers that were presented at the IUTAM Symposium on *Computer Models in Biomechanics: From Nano to Macro*, which was held at Stanford University, California, USA, from August 29 to September 2, 2011. The setting of Stanford University in Palo Alto and the San Francisco Bay Area of California is a rich melting-pot of culture, and an area with probably the highest density of stimulating experts and pioneers in the world, hence it is a magical place which has a lot to offer and which was very appropriate for the symposium. For example, in the 120 years since its founding, Stanford University has been home to 26 Nobel Laureates, 16 of whom are still alive. Palo Alto is also home to a number of high-tech Silicon Valley companies including Hewlett-Packard, founded by two Stanford graduates in a one-car garage in Palo Alto, and the biggest social-networking site, Facebook.

The IUTAM Symposium brought together 68 participants from universities, research centers and clinics in 14 countries. There were 35 invited oral presentations, including 5 keynote lectures to open the morning sessions throughout the week, and 33 young researchers to give poster presentations on the second afternoon of the meeting. The keynote lectures were given by P. Fratzl (Max Planck Institute, Potsdam, Germany), P. Hunter (University of Auckland, New Zealand), L. Taber (Washington University, St. Louis, USA), and A. Yoganathan (Georgia Institute of Technology, USA), while K. Parker (Harvard University, USA) could not come to give his keynote lecture due to the Hurricane Irene.

The computational modeling of biomechanics and mechanobiology is one of the most exciting multidisciplinary areas of this century. It is a rapidly expanding research area which involves researchers in engineering, physics, biology, medicine, applied mathematics and mechanics. Biomechanical modeling and computational simulations in biology hold promise to provide new insight into the complex multiscale and multiphysics phenomena of living tissue: the quantitative analysis of biomechanical processes on the molecular, cellular, tissue, and organ levels might enable reliable predictions of the progression of various types of disease. This may allow us to perform real-time, patient-specific simulations and to guide the design of optimal treatment strategies. The IUTAM Symposium aimed to bring together

young researchers and the world's leading experts working in the field, to provide a forum for discussion and to stimulate the study of challenging new topics in computational biomechanics.

One important aim was to provide computer algorithms, and the skill for implementations of biomechanical models in numerical codes; and this is essential because of the complexity of the materials and the geometries encountered in applications. Efficient computer models at the molecular, cellular, tissue and organ levels are key to better understand inter-relations between coupled processes such as growth, remodeling, and repair, and how mechanical information is processed and programmed by the cells (mechanobiology). Efficient computer models are one of the prerequisites for effective design and development of soft and hard tissue prostheses. Thematically, the IUTAM Symposium revealed a number of exciting new trends; several new aspects have been discussed in detail, which distinguish living biological materials from standard engineering materials such as adaptive responses (growth, remodeling) and active responses (force generation due to muscle contraction).

This volume includes topics on:

- *Protein and Cell Mechanics*

One of the most promising trends to accurately characterize biomechanical phenomena is to explore their responses on the cellular level and to generate related computer models. Observations on the microscopic scale provide additional information, and, ideally, these observations feed back to macroscopic models that help to explain the biomechanical response of the overall tissue or organ. In the present volume this area is covered by the suggestion of a coarse-grained model for unfolded proteins, a collagen-proteoglycan model to capture the structural interaction in the human cornea, and a model to predict the values of forces generated by cells adhered on flat gels and on beds of micro-posts of variegated stiffness.

- *Muscle Mechanics*

Computational models for smooth, cardiac and skeletal muscles are presented. In particular, a mathematical approach for studying Ca^{2+} -regulated smooth muscle contraction is reviewed and the chemomechanical model is implemented into a finite element (FE) program; 3D boundary-value problems are solved and the model is validated by experiments on porcine smooth muscle tissue strips. Finally, in regard to smooth muscle contraction, a homogeneous model is illustrated by using a continuum thermodynamical framework. An actomyosin model is studied to capture the mechanical contraction and energy consumption by the cardiomyocytes. Finally, two skeletal muscle models are presented; one is on the basis of electromechanics and the other combines principles of multi-body dynamics with continuum mechanics and the FE method to achieve a 3D forward-dynamics model of the musculoskeletal system.

- *Cardiovascular Mechanics*

This topic is of major interest and is the most extensive area covered in this volume. It includes a review of continuum level models of arterial adaptations, their validations, and suggests an approach to incorporate molecular level information

within such models. The next chapter presents an experimental and computational framework to define and predict damage due to mechanical loading with an application to arterial clamping. Two chapters are devoted to aneurysms, in particular to the evaluation of dissection properties of human ascending thoracic aortas and to a computational methodology to remove an intracranial aneurysm and reconstruct the geometry of the healthy artery; a fluid-solid-growth framework for modeling aneurysm evolution is also outlined and its application to clinical cases illustrated. Two chapters focus on the mathematical modeling and computation of electromechanical mechanisms in the heart by considering the anisotropy of myocardial tissue. A computational fluid-solid-interaction model investigates possible effects on the hemodynamics within thoracic aorta and coronary, carotid and cerebral arteries due to a distal aortic coarctation. The last chapter within this topic shows the importance of combining medical imaging, computer graphics and computational fluid simulations to better guide surgical interventions such as the Fontan procedure.

- *Multiphasic Models*

The next key topic deals with computational models required to analyze biological mixtures consisting of a porous (neutral and charged) deformable solid matrix and interstitial solvent and solutes. It starts by describing some features of the open source finite element program FEBio and continues with the presentation of an alternative approach to mixture theory-based poroelasticity in order to establish a basis for the development of constitutive equations for growth of tissues. A multiphasic modeling approach is used to analyze brain tissues considered as an elastic solid skeleton which is perfused by two liquids, the blood and the interstitial fluid. Special attention is focused on tumor therapies carried out by convection-enhanced delivery processes; 2D and 3D examples are discussed. A 3D computational model for remodeling of microperfusion is also presented. The biphasic model is based on the theory of porous media; application is shown by covering microcirculation in liver lobes. Next, the effectiveness of mechano-transport coupling in simulating biological growth, in particular tumor growth dynamics, is demonstrated. Thereby, the effectiveness of tools such as adaptive mesh refinement and automatic differentiation is also demonstrated. Finally, crack growth in a swelling porous medium such as the intervertebral disc is numerically analyzed and two options are discussed to account for the sharp pressure gradient around the crack.

- *Morphogenesis, Biological Tissues and Organs*

Another challenging and trend-setting topic is the computational biomechanics of morphogenesis and development of various morphogenetic processes. Here, recent advances of the physical mechanisms of morphogenesis during brain development, in particular the formation of the primary brain vesicles and folding of the cerebral cortex, is discussed. Finally, mechanical characterization and predictive computer models of native and engineered anterior cruciate ligaments (ACLs), human liver, bone and lung are presented. In particular, a micromechanical constitutive model is reviewed to capture the inhomogeneous, nonlinear viscoelastic properties of native ACLs and of tissue engineered ligament grafts

upon explantation. Characterization of the *in vivo* mechanical behavior of human liver is conducted during open surgery using an aspiration device, and related histopathology is identified with biopsies taken at the measurement locations. Next, an *in vivo* validation framework for tissue level models such as bone remodeling and mechanobiology, based on true geometries, is analyzed. Finally, different types of overall lung models are reviewed concluding with an approach that couples 3D and lumped airway models.

The IUTAM Symposium provided scientific impetus, a good basis for generating new ideas for future research directions and some cultural impressions. It has also provided a unique forum to discuss mathematical equations that characterize (sub)cellular responses, specific biological tissues and computational tools that can be used to simulate their complex spatial and temporal responses. It created exciting new synergies and initiated new collaborations across disciplines and between young researchers and the world's leading experts in molecular, cellular, tissue, and organ biomechanics to shape pathways for the future multiscale and multiphysics modeling of biomechanical phenomena.

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