**DGM expert committee Modelling, Simulation and Data**

Research group Microstructural Mechanics

The fall meeting with the topic

# Biomechanics and Biomaterials

**15 November 2023**

Department of Structural Mechanics and Analysis (SMB)

Technische Universität Berlin

Prof. Dr.-Ing. Sandra Klinge, TU Berlin

Prof. Dr. Alexander Hartmaier, Ruhr-Universität Bochum

**Microstructural Mechanics meeting**

**within the DGM expert committee Modelling, Simulation and Data**

Wednesday, 15 November 2023

TU Berlin, MS-building, room 107, Einsteinufer 5, 10587 Berlin

Access via Zoom using this Link
Meeting-ID: 644 1684 9072, Kenncode: 319096

M E E T I N G  P R O G R A M M

| | |
|---|---|
| 09:30-10:00 | Arrival |
| 10:00-10:15 | Opening and introduction of participants |
| **10:15-11:15** | **Session 1 (Material and tissue engineering)**<br>*1 Marc Graham: Multiscale Homogenisation of Diffusion in Calcified Hydrogels (TU Berlin)*<br>*2 Charis Czichy: Description of the deformation behaviour of magnetic Hydrogels (TU Dresden)*<br>*3 Christian Bleiler: Combining Analytical Homogenisation Schemes and Soft Tissue Mechanics: A Multiscale Framework for Skeletal Muscle Tissue (Uni Stuttgart)* |
| 11:15-11:30 | Break |
| **11:30-12:30** | **11:30-12:30 Session 2 (Hard tissue)**<br>*4 Dirk Steglich: Strength and Ductility Loss of Magnesium-Gadolinium due to Corrosion in Physiological Environment (Helmholtz-Zentrum hereon)*<br>*5 Katharina Immel: Modeling the debonding of osseointegrated implants due to coupled adhesion and friction (RWTH Aachen)*<br>*6 Uwe Wolfram: Multi-modal imaging-based computational bone strength assessment incorporating pre-existing 'hidden' microporosity (TU Clausthal)* |
| 12:30-13:30 | Lunch |
| **13:30-14:30** | **13:30-14:30 Session 3 (Soft tissue 1)**<br>*7&8 Marlon Suditsch: Continuum-mechanical and data-driven simulations of brain tumours (Uni Stuttgart)*<br>*9 Phoebe Szarek: Inverse Micromechanical Analysis of Networked Type II Collagen Fibers in Articular Cartilage (University of Connecticut)* |
| 14:30-14:45 | Break |
| **14:45-15:45** | **Session 4 (Soft tissue 2)**<br>*10 Yongjae Lee: A computational method for simulating myocardial growth and pathological ventricular remodelling in human heart models (TU Dresden)*<br>*11 Jianye Shi: Multi-physical modeling of coronary in-stent restenosis (RWTH Aachen)*<br>*12 Melika Mohammadkhah: Exploring the reason for tension and compression stress-strain asymmetry observed in passive skeletal muscle (TU Berlin)* |
| 15:45-16:00 | Closing |

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# ABSTRACTS

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# Multiscale Homogenisation of Diffusion in Calcified Hydrogels

M. Graham[1], S. Klinge[1]

[1] Technische Universität Berlin

While hydrogels can be tuned to have favourable mechanical properties (e.g. strength and toughness) when dry, in most cases these qualities are lost when the hydrogel is swollen with water. To date much work has been done to coat the hydrogels or to develop hydrophobic gels and protect them from water but the recent development of calcified hydrogels by enzymatic mineralisation of calcium into the gels has achieved impressive mechanical properties approaching those of biological tissues such as skin and cartilage. These relatively new materials have a heterogeneous structure and show complex diffusion behaviour, which is a relevant feature in biomedical applications, especially when cell cultures are hosted on the hydrogel substrate.In order to study this application-relevant property of hydrogels, the present contribution uses the homogenisation method based on a two-scale asymptotic expansion. The chosen procedure yields a homogenised diffusion tensor in terms of the volume average of its original counterpart and of solutions of auxiliary problems for unit perturbations and periodic boundary conditions. The latter are solved by using the finite element method and software library deal.II.The contribution particularly focuses on two types of microstructures. In the first case, amorphous calcium phosphate aggregates in semi-porous spheres throughout the hydrogel matrix, and in the second case the calcium forms a double inorganic-organic network. Accordingly, the representative volume elements (RVE) differ: The RVE of the first material type includes spherical, semi-permeable obstacles that are randomly distributed over the matrix material with a higher diffusivity. The situation is opposite concerning double-network hydrogels. Here, the matrix material is impermeable, whereas, the interconnectivity of pores is decisive for the effective diffusivity of the whole composite. The presentation compares the effective diffusivities of different materials for different size of diffusing macromolecules (proteins) as the final result.

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# Description of the deformation behaviour of magnetic hydrogels

C. Czichy[1], S. Odenbach[1]

[1] Technische Universität Dresden

Research in the field of tissue engineering for implants is recently focusing on cell-laden scaffolds. The objective is to facilitate cell growth and differentiation processes through the application of cyclic stimulation to the samples. Our proposal involves using a biodegradable hydrogel containing magnetite microparticles. This hydrogel can be deformed contactless using a magnetic field gradient. To characterise the deformation behaviour of the material, instead of complex structures such as scaffolds we look at a cylindrical bending beam as a simple and reproducible system. The bending curve $w$ depends on the coordinate $y$, which is in the longitudinal direction of the sample, and can be described with $w(y) = \left\{\frac{q\,l^4}{24\,EI_x}\right\}\left(\frac{y}{l} - \frac{2y^3}{l^3} + \frac{y^4}{l^4}\right)$. (1) Thereby $I_x$ is the moment of inertia, $E$ is the Young's modulus, and $q$ is a linear load over the whole length $l$ of the sample with $q(y) = F\,l = constant$. (2) It based on the simplified equation for the Kelvin force $F = \mu_0 V\,M_V \nabla H$ (3)with the magnetic permeability of the vacuum $\mu_0$, the volume $V$ of the sample, the volume magnetisation $M_V$ and the magnetic field gradient $\nabla H$. Using an experimental setup with a Maxwell configuration for a $\mu CT$, the actual bending curve depending on particle concentration and date can be detected. These measured curves are compared with the calculated bending curve.In addition, series of images capturing the deformation process during the application of the magnetic field gradient were obtained using $\mu CT$. These image series provide insights into the time-dependent behaviour. Multiple experiments were conducted to analyse the step response, allowing us to develop an approach for it and determine initial parameters.

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# Combining Analytical Homogenisation Schemes and Soft Tissue Mechanics: A Multiscale Framework for Skeletal Muscle Tissue

C. Bleiler[1], P. Ponte Castañeda[2], O. Röhrle[1]

[1] Universität Stuttgart
[2] University of Pennsylvania, Philadelphia (United States)

Biological soft tissues are—from a mechanical point of view—fascinating composite structures with properties that are optimally adapted to the manifold functions in the body. In skeletal muscles, for example, elastin and collagen fibres provide flexibility and stability when needed. Moreover, through the muscle fibres, they show the ability to convert chemical energy into mechanical energy and are thus the essential component of the musculoskeletal system to perform voluntary movements.The continuum-mechanical modelling of skeletal muscle tissue requires the resolution of intra- and inter-subject-specific properties of the tissue. This is especially true for the modelling of pathological tissue. Thus, the authors proposed a multi-scale framework [1] that takes into account the relevant microstructural components and their arrangement. In a next step, we merged the muscle model—that originally relies on an affinity assumption—with an analytical homogenisation method [2]. The homogenisation scheme is based on the tangent-second-order method [3] and provides an excellent balance between accuracy and simplicity. It is generally applicable to a wide range of materials, be it biological tissues or man-made materials. Particularly, we formulated estimates for fibrous composites two-phase composites with anisotropic phases.The proposed setup that combines a generally applicable homogenisation method and the direct biomechanical application enables comprehensive studies on the influence of nonaffine micro-deformations on the macroscopic tissue-level response in skeletal muscle tissue. This is of particular importance when the muscle model is embedded in computationally demanding large-scale simulations consisting of several muscles, because it possibly allows to use the simpler affine model whenever possible.

References:

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# Strength and Ductility Loss of Magnesium-Gadolinium due to Corrosion in Physiological Environment

D. Steglich[1]

[1] Helmholtz-Zentrum hereon GmbH, Geesthacht

Magnesium (Mg) and its alloys are becoming increasingly popular as alternatives to permanent implant materials due to their biodegradability, biocompatibility and ability to promote bone growth. We propose a computational framework to study the effect of corrosion on the mechanical strength of magnesium samples. Our work is motivated by the need to predict the residual strength of biomedical Mg implants after a given period of degradation in a physiological environment. To model corrosion, a mass-diffusion type model is used that accounts for localised corrosion using Weibull statistics. The overall mass loss is prescribed (e.g., based on experimental data). The mechanical behavior of the Mg samples is modeled by a state-of-the-art Cazacu-Plunkett-Barlat plasticity model with a coupled damage model. This allowed us to study how Mg degradation in immersed samples reduces the mechanical strength over time. We performed a large number of in vitro corrosion experiments and subsequent mechanical tests to validate our computational framework. Our framework could predict both for tension and compression tests the experimentally observed loss of mechanical strength and ductility due to corrosion. Our study confirmed that it is important to consider the surface/volume effect of the samples during corrosion testing and numerical analysis.

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# Modeling the debonding of osseointegrated implants due to coupled adhesion and friction

K. Immel[1], G. Haiat[2]; V.-H. Nguyen[2]; R. Sauer[3]

[1] Forschungszentrum Jülich GmbH, Aachen
[2] MSME, CNRS UMR 8208, Université Paris-Est Créteil, Université Gustave Eiffel (France)
[3] University of Technology, Gdańsk (Poland)

Cementless bone implants have become widely used for replacement surgery. The initial stability of these implants is established during the surgery, through a press-fit in the host bone. The long-term stability of these implants is achieved by bone growing around and into the rough surface of the implant, a process called osseointegration. However, debonding of the bone–implant interface can still occur due to aseptic implant loosening and insufficient osseointegration, which may have dramatic consequences. The aim of this work is to describe a new 3D finite element frictional contact formulation for the debonding of partially osseointegrated implants. The contact model is based on a modified Coulomb friction law, that takes into account the tangential debonding of the bone-implant interface. This model is extended in the direction normal to the bone-implant interface by considering a cohesive zone model, to account for adhesion phenomena in the normal direction and for adhesive friction of partially bonded interfaces. The model is applied to simulate the debonding of an acetabular cup implant, a part in partial and total hip joint replacements. The influence of partial osseointegration and adhesive effects on the long-term stability of the implant is assessed. Furthermore, the influence of different patient- and implant-specific parameters such as the interface friction coefficient, the trabecular Young's modulus, and the interference fit is also analyzed, in order to determine the optimal stability for a specific patient.

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# Multi-modal imaging-based computational bone strength assessment incorporating pre-existing ‘hidden’ microporosity

U. Wolfram[3], S. McPhee[1]; L. Kershaw[2]; C. Daniel[2]; M. Peña Fernández[1]; S. Taylor[2]

[1] Heriot-Watt University, Edinburgh (United Kingdom)
[2] University of Edinburgh, Edinburgh (United Kingdom)
[3] Technische Universität Clausthal

Introduction: Microdamage accumulated by cyclic loading or single overloading events contributes to bone fragility through a reduction in stiffness and strength [1]. QCT-based computational modelling cannot incorporate existing in vivo microdamage due to limited resolution. MR imaging on the other hand, is sensitive to pathophysiological changes to adjacent bone marrow that is ‘hidden’ to clinical CT imaging. In the case of repetitive trauma, signal hyperintensity in fluid sensitive sequences is indicative of a stress response where edema, haemorrhage and hyperaemia are present alongside microdamage [2]. Here, we aim to quantify this signal hyperintensity and use it to derive a pre-existing damage variable that represents the underlying tissue damage prior to overloading. We incorporate this variable into a constitutive model to investigate its influence on material and whole bone stiffness and strength.Materials and Methods: We use the equine athlete as a model for microdamage induced stress fracture where high-speed exercise induces subchondral microdamage. Distal metacarpals (MC3) from n=5 Thoroughbred racehorses were scanned by clinical QCT (0.3 mm voxel size), calibrated to bone mineral density (BMD) and converted to bone volume fraction (BV/TV). MR images (T1w, STIR) were acquired at 3T (0.3 mm voxel size) and registered to the QCT data. Regions of ‘dense’ or ‘sclerotic’ subchondral bone, where microdamage coalesces [3], were segmented from T1w images. Patch-based similarity [4] was used to generate pseudoCT (pCT) images from STIR images. A relative increase in STIR intensity in the dense subchondral bone returned a lower pCT-derived BMD than QCT. This reflects the presence of underlying porosities such as microdamage and increased vasculature [2]. We derived a pre-existing damage variable (Dpex) which affects stiffness and strength and incorporated it into an isotropic, asymmetric BV/TV-dependent elasto-viscoplastic material model (UMAT, Abaqus v6.16) [5,6,7]. Voxel based FEA was used to compress MC3 condyles in silico before (Dpex=0) and after the inclusion of accumulated ‘hidden’ porosity (Dpex>0) to investigate its influence on whole bone mechanical properties. Results: pCT BMD in dense subchondral bone was lower in all MC3 bones. Incorporating D^pex resulted in a median reduction of material stiffness and strength of 20.3% and 20.9% in tension and compression. Inclusion of Dpex reduced whole bone stiffness and strength, and their reduction correlated with Dpex (R2=0.74, R2=0.89). Previous experimental results support our interpretation [8,9]. Discussion: We propose a methodology for incorporating MRI signal hyperintensity into QCT-based FE models to include pre-existing porosities that cannot be detected by clinical CT. While our results illustrate the value of multimodal imaging to potentially capture existing microdamage in vivo, this concept requires validation by histologic evidence – which is our next step. However, as we use clinical imaging techniques, our results may also aid research in diseases such as osteoarthritis and bone cancer.

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# Continuum-mechanical and data-driven simulations of brain tumours

M. Suditsch[1], T. Ricken[1]; A. Wagner[1]

[1]Universität Stuttgart

A short remaining life expectancy and high mortality characterise brain tumours as a particularly dangerous disease. Simulations of the relevant processes of tumour growth and regression in brain tissue are realised by a continuum-mechanical model in the framework of the Theory of Porous Media (TPM), that is embedded in a data-integrated workflow. This workflow is based on suitable patient-specific data, that is basically available, e. g. from magnetic resonance images (MRI). Preparing the data by a set of tools, for example using a convolutional neural network in a shape of an U-Net, result in the segmented position and composition of the tumour and provide the referential geometry of an initial boundary value problem (IBVP). Furthermore, relevant information, e. g. about heterogenities or flow properties, are collected by image-processing tools. A more cost effective surrogate model based on the ratio of the composition of the tumour compartments is developed and calibrated with simulations of the TPM model. These modularly arranged components of the developed data-integrated approach are processed using the finite-element framework FEniCS and allow to study relevant clinical questions.

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# Inverse Micromechanical Analysis of Networked Type II Collagen Fibers in Articular Cartilage

P. Szarek[1], D.M. Pierce[1]

[1]University of Connecticut, Storrs, CT (United States)

The mechanical responses of most soft biological tissues rely heavily on networks of collagen fibers, thus quantifying the mechanics of individual fibers and networks of fibers advances understanding of tissues in health and disease. In articular cartilage, type II collagen fibers exhibit depth-dependent orientations and diameters, contributing to the unique heterogeneous mechanics essential to its the mechanical function. Osteoarthritis (OA), a disease affecting a growing number of people, alters the morphology of the collagen network which, in turn, compromises the transfer of load through the musculoskeletal system. We first quantified the zone-specific morphology of collagen in human cartilage during early OA. We used transmission electron microscopy to directly observe individual fibers (~20-200 nm in diameter) and custom image analyses to quantify distributions in principal orientation, dispersion, and diameter of collagen fibers in the early grades of OA in each through-thickness zone. We then established experimental methods to study type II collagen fibers within a native networked structure. We systematically investigated mechanical tests of networks of type II collagen undergoing uniaxial extension to failure, quantifying ranges for each of the key experimental variables (e.g. specimen thickness, strain rate) to best ensure that the procedure itself does not affect the measured mechanical behaviors. Finally, we established the first data-driven constitutive model of the stress-stretch and failure of type II collagen leveraging tensile testing of networks of type II collagen, inverse finite element analyses, and statistically equivalent representative volume elements (SERVEs) based on our quantitative morphological data. Our results provide fundamental data and understanding, and aid in improving models of tissues containing type II collagen and models of tissue damage and degeneration at the microstructural level.

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# A computational method for simulating myocardial growth and pathological ventricular remodelling in human heart models

Y. Lee[1], B. Cansız[1], M. Kaliske[1]

[1]Technische Universität Dresden

In this study, we introduce a novel three-dimensional constitutive model that describes the electro-visco-elastic-growth response of the myocardium with a fully implicit staggered solution procedure for the strong electromechanical coupling.This novel approach allows us to simulate and analyze the cardiac remodelling in actively contracting human ventricular heart models, which is characterized by a growing viscoelastic myocardium, where the growth direction is determined based on the mechanical state of each element at each time step. A multiplicative decomposition method is adopted for the total deformation gradient into two main parts: a mechanical-active part and a growth part. The mechanical-active component is further divided into elastic, viscous, and active components.To ensure unconditional stability during time integration, a backward Euler integration scheme is used. Our developed model enables us to observe two types of growth within the myocardium: stretch-driven longitudinal (fibre) growth and stress-driven transverse (cross-fibre) growth. These capabilities provide valuable insights into how different mechanical impacts affect heart tissue development.To validate the effectiveness of the developed approach, two distinct simulations related to pathological ventricular remodelling are conducted: one involving two divergent types of remodelling in a left ventricular model driven by hemodynamic overloads; another examining ventricular remodelling initiated by acute myocardial ischemia within a biventricular heart model.These simulations not only demonstrate the new method's applicability but also highlight its potential for advancing our understanding of complex cardiac conditions and their impact on heart structure and function.

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# Multi-physical modeling of coronary in-stent restenosis

J. Shi[1], K. Manjunatha[1]; S. Reese[1]

[1]RWTH Aachen University

Coronary artery disease (CAD) is one of the largest causes of death worldwide. Percutaneous coronary intervention (PCI) is one of the minimally invasive procedures used to overcome CAD by restoring blood flow in clogged coronary arteries. Unfortunately, PCI is associated with several risk factors including in-stent restenosis and stent thrombosis. Drug-eluting stents have been developed to counteract the severe restenosis observed after bare-metal stent implantation. However, the risk of restenosis still prevails due to the inhibitory effect of the drug on endothelial healing. The current work focuses on developing a multiphysics model using both continuum and deep learning framework to describe the in-stent restenosis, including the effect of anti-inflammatory drugs embedded in the drug-eluting stents.

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# Exploring the reason for tension and compression stress-strain asymmetry observed in passive skeletal muscle

M. Mohammadkhah[1], P. Murphy[2]; C. Simms[2]; S. Klinge[1]

[1]Technicshe Universität Berlin
[2]Trinity College, Dublin (Ireland)

For many years, only the force producing capabilities of skeletal muscle was of interest. However, the mechanics of passive skeletal muscle are important in many biomechanical applications such as impact biomechanics and rehabilitation engineering. An adequate explanation for the tension/compression asymmetry observed in the stress-strain response of skeletal muscle and the role of Extra Cellular Matrix (ECM) as a contributor to stress response remains elusive. Therefore, the overall aim of this study is to advance the knowledge of the passive mechanical behaviour of skeletal muscle, and its relation to the microstructure of the muscle through combined experimental, microstructural and computational approaches. From the experimental point of view, mechanical testing of skeletal muscle of chicken and porcine tissue was conducted to observe the different stress-strain asymmetry between species. Since collagen in ECM is the main structural protein in connective tissues, it is believed to be primarily responsible for their passive load-bearing properties. The optimised protocol of visualisation of collagen was applied to report qualitatively and quantitatively on skeletal muscle ECM reorganization during applied deformation using a combination of CNA35 binding protein and confocal imaging of tensile and compressive deformation of porcine and chicken muscle samples applied in both the fibre and cross-fibre directions. Results show the overall three-dimensional structure of collagen in perimysium visible in planes perpendicular and parallel to the muscle fibres in both species. Furthermore, there is clear evidence of the reorganization of these structures under compression and tension applied in both the muscle fibre and cross-fibre directions, which generally explains anisotropy observed in the stress-strain response for both tissues. These observations improve our understanding of how perimysium responds to three-dimensional deformations. The three-dimensional illustration of perimysium structure was then used as a basis to create a microstructural-geometrical model to predict the passive mechanical stress-strain response observed in skeletal muscle. The current model represents the whole muscle response as a combination of both a group of muscle fibres (fascicle) response and the perimysium (ECM) response. It shows that although perimysium was believed to be a key element in the muscle stress response, the muscle fibres also contribute to stress-stretch response since the order of magnitude for the stress in muscle fibres is similar to that of perimysium. The model yields a good prediction of the whole muscle behaviour in Tension-Fibre and Compression-Fibre deformations using the optimum values for the model parameters obtained from the sensitivity studies.