Doctoral Dissertation
Doctoral Program in Matematica Pura e Applicata (37.th cycle)

Computational and theoretical problems in fractional and higher-order theories for modeling biomechanical media

Alessandro Giammarini

* * * * *

Supervisor
Prof. Alfio Grillo

Politecnico di Torino
July 24, 2025

I hereby declare that, the contents and organisation of this dissertation constitute my own original work and does not compromise in any way the rights of third parties, including those relating to the security of personal data.

. . . .

Alessandro Giammarini
Turin, July 24, 2025

Synthesis of the Thesis

The following text is an extract from the Introduction of my PhD Thesis

This Thesis focuses on the modeling and simulation of some classes of multi-constituent biological media by introducing appropriate mathematical tools to deal with the non-local and multi-scale aspects that characterize their mechanical behavior. In particular, the Thesis is divided in three parts, each corresponding to a problem of biomechanical relevance, and to a different approach in the mathematical description of the interactions within the system under investigation. In particular, these mathematical tools include fractional calculus, higher order theories in the anelastic descriptor, two-scale Asymptotic Homogenization techniques and elements borrowed from Statistical Mechanics. The resulting problems are inherently non-linear, fully coupled, and solve numerically some benchmarks to gain insight from the simulations.

Part I. *The work reported in this part has been previously published in [1] and [2].*

Part I comprises the studies related to the mechanics of hydrated, fluid-saturated porous media for the description of biological tissues, here described as solid-fluid mixtures, in which the tissue undergoes phenomena of reorganization of its inner structure. Such processes, which result in an alteration of the biomechanical property of the material, are identified as *remodeling* phenomena in the Biomechanical community. The manifestations of remodeling and its coupling with the fluid flow constitute the main areas of investigation of this Part.

In Chapter 1, we start by discussing the main modeling hypothesis and we present the balance laws and the modeling equations governing the dynamics of a solid-fluid mixture. Moreover, we refer to the Theory of Elasto-Plasticity to introduce the remodeling descriptors via the Bilby-Kröner-Lee decomposition.

Chapter 2 introduces briefly the topic developed within, which is the study of the remodeling of multicellular aggregate, and outlines the most relevant features of the experimental procedure.

In particular, we present a mathematical model of the compression of multicellular aggregates and we specialize it to a compression-release test that is well known in the biological literature. Within the adopted mechanical setting, a multicellular aggregate is studied as a biphasic system consisting of a soft solid porous medium saturated with an interstitial fluid. In particular, together with the deformation of the considered aggregate, the characterization of the model outlined in this work relies on four fundamental features. First, by assuming the interstitial fluid to be macroscopically inviscid and to evolve according to the Darcian regime, we resolve its flow and determine the associated time dependent pressure distribution. Second, we focus our attention on the remodeling of the compressed aggregate, that is, on the rearrangement of its internal structure in response to the external loads applied to it. Specifically, we look at the way in which such a rearrangement is induced by the considered experiment and at how it affects the mechanical behavior of the aggregate. Moreover, we introduce a remodeling-dependent permeability tensor with the purpose of visualizing a more direct influence of remodeling on the dynamics of the aggregate's interstitial fluid. Finally, we resolve the interactions exchanged between the aggregate and the compressive apparatus. This task necessitates the formulation of an appropriate contact problem, thereby calling for the description of the evolution of the area through which the aggregate and the apparatus exchange mechanical interactions. In particular, the continuity conditions to be applied on such a contact area are discussed. Our numerical simulations show the role played by the different phenomena accounted for in the model and the overall dynamics of the aggregate within the considered experiment.

Chapter 3 specializes the study of hydrated tissues to the case of articular cartilage, here thought as a tri-phasic mixture composed of solid extracellular matrix, solid fibers and intracellular fluid.

We present a mathematical model for the reorientation of fibers in a soft, fiber-reinforced, fluid-saturated porous medium describing a hypothetical biological tissue. We consider two types of remodeling that, at different scales, concur in determining the structural reorganization of the solid phase of the medium: one pertains to the development of plastic-like distortions, which are introduced as the macroscopic manifestation of processes occurring at lower scales, but not resolved explicitly; the other one, originating at the mesoscale, concerns the capability of the fibers of reorienting in the extracellular matrix. This latter form of remodeling is studied as a Langevin-like process in which two main agencies are recognized: a drift term, which is given by the effects that the deformation of the extracellular matrix exerts on the fibers; a noise term, which accounts for the interactions among nearby fibers. We employ the framework of the Principle of Virtual Power (PVP) to present our model, in which we "free" the kinematics of the system from the constraints of isochoricity of remodeling and incompressibility of the mixture by appending the Chetaev forms of these constraints to the PVP. Then, we specialize our model to articular cartilage. We do this for comparing our results with some experimental curves describing the distribution of collagen fibers in a sample of articular cartilage, and for studying, through the simulation of a uniaxial compression test, the interplay between fluid flow and the two aforementioned forms of remodeling. Our main result is the establishment of a framework that captures effectively the mechanical coupling between the fiber distribution specific to a given medium and the mechanical stimuli exerted on such distribution. Quite differently from other works on this subject, our framework is capable of accounting for the stochastic effects of the fibers on the overall evolution of the considered tissue.

Part II. *The work reported in this part has been previously published in [4].*

In Part II we propose a model of fluid flow by describing it with a *fractional version* of *Forchheimer's correction* to Darcy's law. In fact, Darcy's law is a simplified flow model that puts the pressure gradient and the mixture filtration velocity, which is a quantity proportional to the difference between the fluid and the solid velocity, in a linear relation, and is often employed in the description of fluid saturated media.

Chapter 4 presents a theoretical and numerical study of the flow of the interstitial fluid saturating a porous medium, principally aimed at modeling a bio-mimetic material and assumed to experience a dynamic regime different from the Darcian one, as is typically hypothesized in biomechanical scenarios. The main aspect of our research is the conjecture according to which, for a particular mechanical state of the porous medium, the fluid exhibits two types of deviation from Darcy's law. One is due to the inertial forces characterizing the pore scale dynamics of the fluid. This aspect can be resolved by turning to the *Forchheimer correction* to Darcy's law, which introduces non-linearities in the relationship between the fluid filtration velocity and the dissipative forces describing the interactions between the fluid and the solid matrix. The second source of discrepancies from classical Darcy's law emerges, for example, when pore scale disturbances to the flow, such as obstructions of the fluid path or clogging of the pores, result in a time delay between drag force and filtration velocity. Recently, models have been proposed in which such delay is described through constitutive laws featuring fractional operators. Whereas, to the best of our knowledge, the above-mentioned behaviors have been studied separately or in small deformations, we present a model of fluid flow in a deformable porous medium undergoing large deformations in which the fluid motion obeys a fractionalized Forchheimer's correction. After reviewing Forchheimer's formulation, we present a fractionalization of the Darcy-Forchheimer law, and we explain the numerical procedure adopted to solve the highly non-linear boundary value problem resulting from the presence of the two considered deviations from the Darcian regime. We complete our study by highlighting the way in which the fractional order of the model tunes the magnitude of the pore pressure and fluid filtration velocity.

Part III. *The work reported in this part has been previously published in [3].*

In Part III we employ the theory of Asymptotic Homogenization to study the elasto-plastic behavior of a composite medium comprising two solid phases, separated by a sharp interface and characterized by mechanical properties, such as elastic coefficients and "initial yield stresses" (i.e., a threshold stress above which remodeling is triggered), that may differ up to several orders of magnitude. We speak of "plastic" behavior because we have in mind a material behavior that, to a certain extent, resembles plasticity, although, for biological systems, it embraces a much wider class of inelastic phenomena.

In particular, along Chapter 5, we are interested in studying the influence of gradient effects in the remodeling variable on the homogenized mechanical properties of the composite. The jump of the mechanical properties from one phase to the other makes the composite highly heterogeneous and calls for the determination of *effective properties*, i.e., properties that are associated with a homogenized "version" of the original composite, and that are obtained through a suitable averaging procedure. The determination of the effective properties results convenient, in particular, when it comes to the multi-scale description of inelastic processes, such as remodeling in soft or hard tissues, like bones. To accomplish this task with the aid of AH, we assume that the length scale over which the heterogeneities manifest themselves is several orders of magnitude smaller than the characteristic length scale of the composite as a whole. We identify both a *fine-scale* problem and a *coarse-scale* problem, each of which characterizes the elasto-plastic dynamics of the composite at the corresponding scale, and we discuss how they are reciprocally coupled through a transfer of information from one scale to the other. In particular, we highlight how the coarse-scale plastic distortions influence the fine-scale problem. Moreover, in the limit of negligible hysteresis effects, we individuate two viscoplastic effective coefficients that encode the information of the two-scale nature of the composite medium in the up-scaled equations. Finally, to deal with a case study tractable semi-analytically, we consider a multilayered composite material with an initial yield stress that is constant in each phase. Such investigation is meant to contribute to the constitution of a robust framework for devising the effective properties of hierarchical biological media.

Bibliography

[1] S. Di Stefano et al. “An elasto-plastic biphasic model of the compression of multicellular aggregates: the influence of fluid on stress and deformation”. In: *Z. Angew. Math. Phys.* 73 (2022), pp. 79–118. DOI: https://doi.org/10.1007/s00033-022-01692-1.

[2] A. Giammarini, A. Pastore, and A. Grillo. “A model of fiber reorientation in fiber-reinforced biological materials combining statistical and configurational mechanics”. In: *Mathematics and Mechanics of Solids* (In press).

[3] Alessandro Giammarini, Ariel Ramírez-Torres, and Alfio Grillo. “Effective elasto-(visco)plastic coefficients of a bi-phasic composite material with scale-dependent size effects”. In: *Mathematical Methods in the Applied Sciences* 48.1 (Oct. 2024), pp. 926–979. ISSN: 1099-1476. DOI: 10.1002/mma.10367.

[4] Sachin Gunda et al. “Fractionalization of Forchheimer’s correction to Darcy’s law in porous media in large deformations”. In: *Mathematics and Mechanics of Solids* (Aug. 2024). ISSN: 1741-3028. DOI: 10.1177/10812865241252577.

This Ph.D. thesis has been typeset by means of the TEX-system facilities. The typesetting engine was pdfLATEX. The document class was `toptesi`, by Claudio Beccari, with option `tipotesi=scudo`. This class is available in every up-to-date and complete TEX-system installation.