MECHANICAL ENGINEERING I PHYSICS I PRESERVATION OF THE ARCHITECTURAL HERITAGE I SPATIAL PLANNING AND URBAN DEVELOPMENT I STRUCTURAL SEISMIC AND GEOTECHNICAL ENGINEERING I TECHNOLOGY AND DESIGN FOR ENVIRONMENT AND BUILDING I TERRITORIAL DESIGN AND GOVERNMENT I URBAN PLANNING, DESIGN AND POLICY I AEROSPACE ENGINEERING I ARCHITECTURAL AND URBAN DESIGN I ARCHITECTURAL COMPOSITION I ARCHITECTURE, BUILT ENVIRONMENT AND CONSTRUCTION ENGINEERING I ARCHITECTURE, URBAN DESIGN, CONSERVATION OF HOUSING AND LANDSCAPE I BIOENGINEERING I DESIGN I ELECTRICAL ENGINEERING I ENERGY AND NUCLEAR SCIENCE AND TECHNOLOGY I ENVIRONMENTAL AND INFRASTRUCTURE ENGINEERING I INDUSTRIAL CHEMISTRY AND CHEMICAL ENGINEERING I INFORMATION TECHNOLOGY I INTERIOR ARCHITECTURE AND DESIGN I MANAGEMENT ENGINEERING I MATERIALS ENGINEERING I **MATHEMATICAL MODELS AND METHODS IN ENGINEERING**

PhD Yearbook | 2017

Chair:
Prof. Irene M. Sabadini

DOCTORAL PROGRAM IN MATHEMATICAL MODELS AND METHODS IN ENGINEERING

Mathematics is everywhere, represented by equations. Between the atmosphere and the wing of a spaceship, in the blood flowing in an artery, on the demarcation line between ice and water at the poles, in the motion of the tides, in the charge density of a semiconductor, in the compression algorithms of a signal sending images from outer space. The equations represent real problems. The Mathematical Engineer can see and understand the nature of these equations, and can develop models in order to understand their relevant qualities and solve real problems.
This PhD program aims at training young researchers by providing them with a strong mathematical background and with ability to apply their knowledge to the solution of real-world problems that arise in various areas of science, technology, industry, finance, management, whenever advanced methods are required in analysis, design, planning, decision and control activities. PhD students carry our their research both in the development of new mathematical methods and in the implementation and improvement of advanced techniques in connection with specific contexts and applications.
The Faculty of the PhD program is responsible for the organization of the training and research activities of the PhD students. Decisions of the Faculty comply with the requirements and standards of the Doctoral School of the Politecnico di Milano. A Chairman is elected within the Faculty, for representative and coordination activities. Admission of students to the PhD program is decided after examination of the candidates. Students applying to our program must provide their CV, along with reference and motivation letters. After admission, each student is assigned a tutor. The tutor is a member of the Faculty who assists the student in the early stages of his career, especially in the choice of the courses and in identifying a thesis advisor.

The PhD program has a duration of three years. Activities include:

Soft skills courses; specialized courses; research training, including seminars, tutoring activity, participation to workshops/conferences, and scientific publications; development of a doctoral thesis.
At the end of each academic year, the PhD students report to the Faculty about their activity. The students report about attendance of courses and exams (and the corresponding grades), participation in various scientific activities (seminars, conferences, summer schools etc.), planning and intermediate results on their research project and preparation of the PhD thesis, and any other relevant activity. At the annual meeting the students also receive a grade by the Faculty. A negative grade may entail repetition of the current year of doctoral study (with suspension of the grant, if any) or exclusion from the PhD program, depending on the Faculty's decision. Mobility of PhD students to other institutions is strongly encouraged and financial support is provided to this purpose.
Among others, let us mention some typical types of professional skills and possible occupations of the graduated Doctors: analytic and numerical treatment of differential models for physical and industrial problems, quantitative methods in finance and risk management, operations research and optimisation, statistical modelling and data analysis.
Placement of graduated Doctors is expected in the following positions: research and development divisions of businesses, businesses involved in innovative design activities, financial institutions such as banks or insurance companies, public or private research centres, public and/or governmental agencies for social, economical, scientific study, planning or evaluation, Universities.
Since the PhD program in Mathematical Models and Methods in Engineering (formerly, Mathematical Engineering) has been active since the year 2001, we expect that a larger number of institutions and businesses will soon become more and more aware of the professional skills and expertise of graduated doctors.

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MODELLING SPATIAL AND SPATIO-TEMPORAL FIELDS VIA REGRESSION WITH PDE PENALIZATION

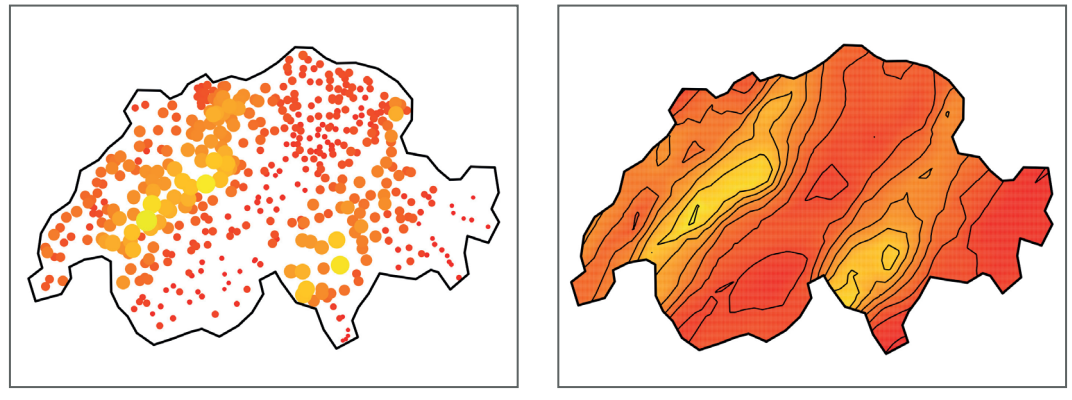
Bernardi Mara Sabina – Supervisors: Prof. Piercesare Secchi, Prof. Laura Maria Sangalli

In this work we develop a class of models for the analysis of spatially distributed data with complex dependencies. In particular, we deal with space-time data distributed over spatial domains with a complex shape, featuring strong concavities and interior holes. Moreover, we consider data characterized by stationary or non-stationary spatial anisotropy. Appropriately taking into account the structure of the complex dependencies present in the data is fundamental to provide accurate estimation for data arising from many fields of sciences, such as physics, biology, meteorology and geology.

The proposed method is based on regularized spatial regression with a penalization involving a partial differential operator. The idea of regularization with differential operators is common in functional data analysis, for instance to tackle the problem of univariate or multivariate curve fitting; a similar approach can be used for the estimation of surfaces or spatial fields. Some examples are given by thin plate splines, soap-film smoothing and bivariate splines. The method proposed in this work interfaces advanced statistical methodology and numerical analysis techniques; in particular, it makes use of the finite element method, which allows to efficiently deal with data distributed over complex domains, including irregularly shaped domains. Furthermore, the method can take into account specific information on the behavior of the phenomenon under study. Indeed, the model can provide estimated fields which satisfy known boundary conditions. Moreover, if covariates are available, they can be accounted for in the model via a semi-parametric framework. This work shows that spatial regression with partial differential regularization can be extended to deal with space-time data observed over complex spatial domains, spatial data characterized by unknown spatial stationary anisotropy, and spatial data characterized by spatial non-stationary anisotropy driven by the texture of the domain. Indeed, three modeling problems are presented, and, in the three cases, three different regularization techniques are proposed.

In the first case, we consider spatio-temporal data defined on a spatial domain featuring strong concavities which affect the phenomenon under study. Classical methods for spatio-temporal data are not well suited for the analysis of this kind of data since they do not take into account the geometry of the domain. In this work we extend the spatial regression with partial differential penalization technique to time dependent data, introducing a regularization which separately takes into account the spatial dimension and the temporal dimension. Simulation studies show the good performances of the proposed model with respect to other spatio-temporal techniques. In particular, the proposed method provides more accurate estimates when the phenomenon under study is influenced by the complex geometry of the spatial domain. The method is applied to the analysis of the temporal evolution of the amount of per capita municipal waste produced in the towns of Venice province. The data are measurements from 1997 to 2011 of the yearly amount of per capita municipal waste (total kg divided by the number of municipality residents) and are provided by the Arpav, the Agenzia regionale per la prevenzione e protezione ambientale del Veneto. The phenomenon is expressed rather differently in different parts of the domain that are close in terms of their geodesic distance, but that are actually separated by the Venice lagoon. Hence, appropriately accounting for the shape of the domain, characterized for instance by a strong concavity formed by the Venice lagoon which is partly enclosed by elongated peninsulas and small islands, is crucial to accurately handle these data. Also in the analysis of these data, the proposed method can properly take into account the complex shape of the domain and is able to capture the temporal evolution of the phenomenon.

In the second case, we analyze data characterized by stationary spatial anisotropy. The method we propose makes use of an anisotropic diffusion operator in the regularization term as to properly take into account the spatial anisotropy present in the data. We consider the smoothing operator as unknown and we estimate it from the data. To this end, we adopt a generalized profiling estimation approach, adapting to our setting the parameter cascading technique. Simulation studies compare the proposed method to both isotropic and anisotropic kriging in various simulation settings showing the good performances of the proposed technique. The method is illustrated via an application to a benchmark dataset of 467 daily rainfall measurements made in Switzerland on the 8th of May 1986; this dataset was used for the Spatial Interpolation Comparison 97. In this applied case, the anisotropy raises from the interaction between geomorphology and atmospheric circulation. Indeed, the data are characterized by a strong spatial anisotropy, with higher rainfall values alternating with lower rainfall values along elongated regions oriented in the northeast-southwest direction. Also in this applied case, the technique is able to capture the right anisotropy, thus providing a good estimated spatial field.In the third case, a method for the analysis of data characterized by non-stationary spatial anisotropy induced by the texture of the domain is presented. In this case, the domain of the phenomenon is not homogeneous, but presents regions with different characteristics which determine a non-homogeneous spatial dependence of the data. The motivating applied problem concerns the estimation of the population mobility in the metropolitan area of Milan from mobile phone data. The domain under study is strongly characterized by the presence of roads, which affect the distribution of the data. Indeed, the phenomenon is characterized by strong anisotropy along the main roads, while it is more homogeneous in the regions without main roads. The method we propose accounts for the non-homogeneity in the spatial dependence of the data by considering, in the penalization term, a non-stationary anisotropic diffusion operator whose anisotropy is estimated from the geometry of the road network characterizing the domain. The estimation of the anisotropy is performed with a technique which models traffic flows in complex networks such as large urbanized areas.



1. Switzerland rainfall data and estimated spatial eld.

REDUCED ORDER MODELS FOR THE PARAMETRIZED CARDIAC ELECTROMECHANICAL PROBLEM

Bonomi Diana – Supervisor: Prof. Alfio Quarteroni

Co-Advisor: Dr. Andrea Manzoni

Cardiovascular diseases currently represent the leading cause of mortality in Europe and are responsible for 45% of all deaths, corresponding to more than 4 millions deaths per year. In order to support the development of new diagnostic and therapeutic techniques, mathematical and numerical models have assumed in the last two decades an important role to investigate the main physical processes related to the cardiovascular system and, in particular to blood flows and cardiac functions, both in physiological and pathological conditions. This thesis focuses on this latter aspect, aiming at the development of efficient numerical strategies for simulating cardiac electromechanics in a wide range of scenarios. Cardiac electromechanical models characterize the interplay between the electrophysiology problem, which describes the propagation of the signal triggering the heart contraction, and the mechanical problem, which describes the contraction and relaxation of the muscle tissue, including the sub-cellular activation-contraction mechanism. Developing efficient computational models is crucial in order to investigate how clinically relevant processes affect different features of the heart beat. In order to take into account the inter-patient variability, the model parameters have to be specifically tuned to fit subject-specific clinical data. To correctly calibrate cardiac models and analyze how the heart contraction depends on parameters of interest several numerical simulations have to be carried out, thus calling into play the need of querying the parameter-to-solution map in a fast and reliable way. Reduced order modeling (ROM) techniques are specifically designed to achieve this goal, as they provide accurate and reliable solutions at a greatly reduced computational cost.
Cardiac electromechanics is a challenging problem from both a mathematical and a numerical viewpoint, because of the coupling of different physical problems which take place at different spatial and temporal scales.
Indeed, a model for the cardiac electrophysiology has to describe on one hand the subcellular activity (1-100μm) which gives rise to the cellular depolarisation, on the other hand the spreading of the electrical signal through the whole myocardium (1-10cm). Moreover, to correctly track the propagation of the wave-front, fine computational grids are needed. The description of the cardiac tissue requires complex constitutive laws, characterized by an exponential strain energy function and by the presence of muscular fibers and sheets, resulting in a complex highly nonlinear model. To describe these processes different works have proposed more and more accurate electromechanical models. However, numerical methods to solve cardiac electromechanical problems are characterized by overwhelming computational costs, thus making the repeated simulation required to tune parameters for model personalization unfeasible if relying only on high-fidelity techniques, such as the finite element method.
The main goal of this thesis is to develop reliable reduced order modeling techniques able to rapidly compute the solution of parametrized coupled electromechanical problems, on both idealized and patient-specific geometries. The reduced order models (ROM) proposed in this thesis will represent a powerful tool in view of performing parameter estimation in a subject-specific framework, sensitivity analyses or uncertainty quantification.
The ROMs proposed in this work rely on the Reduced Basis (RB) method, introduced in the context of nonlinear structural analysis about 40 years ago. The basic idea of the RB method for parametrized PDEs is to seek the solution of such a problem in a subspace of much smaller dimension than the one of the original finite dimensional space employed by a high-fidelity full order model (FOM). Thanks to a suitable computational offline-online decomposition, RB methods are able to provide fast and reliable results at a greatly reduced cost. Being able to approximate the solution at a low computational cost makes the RB method extremely appropriate in many-query contexts, like design optimization, or multi-model/scale simulation. Within this class we can also include cardiac mechanics. For this reason, relying on the RB method provides a twofold advantage when dealing with cardiac mechanics, which has to be solved not only for different parameters, but also at several time instants.
However, the RB method in its classical formulation is no longer efficient when dealing with nonlinear problems, as in the case of the cardiac mechanics. Indeed, when using Newton iterations to solve nonlinear problems, assembling the ROM for any new parameter would require to assemble (also in the online phase) the FOM arrays first and then to project them onto the reduced space, thus calling into play high-fidelity arrays at the online stage, too. To avoid this drawback, we can rely on the so called hyper-reduction techniques to perform system approximation in addition to solution-space reduction, which shall be performed at the same time. In this work the Discrete Empirical Interpolation Method (DEIM) and its matrix version (MDEIM) are combined to perform system approximation, in order to evaluate both the residual vector and the Jacobian matrix very efficiently in the case of complex parametrized nonlinear mechanical problems. We also derive a residual-based a posteriori error estimator which accounts for the errors related to the solution-space reduction and to the DEIM and MDEIM approximations of the finite element residual and Jacobian matrix. Moreover, a purely algebraic approximation of the Jacobian matrix is explored to improve the computational gain.
The efficiency of these techniques is enhanced by the introduction of a new snapshots selection strategy, which we refer to as hybrid method; a comparison of this strategy with two classical methods widely used in the RB literature is provided. Numerical results highlight the dramatic impact of an appropriate snapshots selection strategy on both the computational saving and the accuracy of the reduced solution.
A reduction strategy for the parametrized electrophysiology problem is proposed and special care is devoted to the correct capture of the wave-front propagation featured by the solution of the monodomain equation. We show how to take advantage of DEIM and MDEIM for an efficient tratment of nonlinearities. Besides the nonlinearity, another computational issue that has to be faced is that the electrophysiology problem couples two models; the former for the description of cell activation and the latter for the propagation of the signal. In this work, a proper technique to reduce computational costs associated to the cell model is proposed and an efficient reduction strategy for the two-way coupled problem is derived.
Finally, we address the reduction of the coupled electromechanical problem by properly extending the models developed for both the electrophysiology and the mechanics. Designing an efficient reduction strategy for the electromechanical problem requires to address different level of coupling: at first, the two-way coupling between the nonlinear PDE and the ODEs system constituting the electrophysiology model, and secondly, the one-way coupling between electrophysiology and mechanics, where we neglect the influence of the mechano-electrical feedback. A suitable snapshots selection strategy has been designed to ensure an accurate approximation of the solution of the coupled reduced problem, by splitting the offline stage in two steps.
The efficiency of the proposed ROMs is assessed through numerical experiments performed on both idealized configurations and patient-specific three dimensional geometries.

GAME THEORETIC MODELS OF NETWORK FORMATION A GAME THEORETIC GENERALIZED ADDITIVE MODEL ON NETWORKS: THEORY AND APPLICATIONS

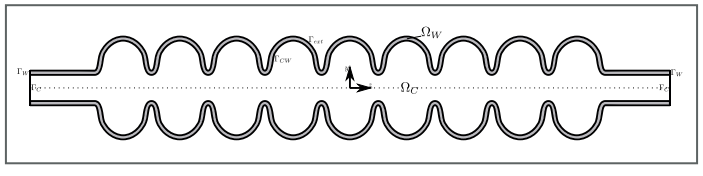
Cesari Giulia – Supervisor: Prof. Roberto Lucchetti

The thesis deals with the theoretical analysis and the application of a new family of cooperative games, where the worth of each coalition can be computed from the contributions of single players via an additive operator describing how the individual abilities interact within groups. Specifically, we introduce a large class of games, namely the Generalized Additive Games, which encompasses several classes of cooperative games from the literature, and in particular of *graph games*, where a network describes the restriction of the interaction possibilities among players.
The motivation for this work comes from the observation that, in many models introduced in the literature, the worth of a coalition of players is strongly related to the sum of the individual values of players over another coalition. This is the case, for example, of the *airport games*, the *argumentation games* and several classes of operation research games, such as the *peer games*, the *maintenance cost games* and the *minimum cost spanning tree games*.
A coalitional game describes a situation in which all players can freely interact with each other, i.e. every coalition of players is able to form and cooperate. However, this is not the case in many real world scenarios and in many cases it is necessary to drop the assumption that all coalitions are feasible. A typical way to model the restriction of the interaction possibilities between players is through a network structure. In *graph games*, a graph (or network) describes the interaction possibilities between players: the nodes of the network are the players of the game and there exists a link between two nodes if the corresponding players are able to interact directly. As an example, in argumentation games, an underlying direct graph describes the attack relations among the arguments in an opinion: there exists an edge from one argument to the other if the former attacks the latter; in mountain situations a rooted directed graph represents the connection possibilities among houses in a village and a source (e.g. a water purifier): there is a link between a house and a lower one if it is possible to connect them in order to create a channel that allows the water to reach the source.
The network structure models the restrictions of the interaction possibilities among players, thus determining how the individual abilities interact within groups of players: if we define the value of a coalition of arguments as its self-consistency, i.e. the number of arguments that are not attacked by another argument in the coalition, then a player in an argumentation game would contribute to a coalition it belongs to only if none of his attackers belongs to the coalition; a house in a mountain situation would contribute to the division of the cost of connection to the source only if it lies on the minimum cost tree connecting the players to the source. In other words, in many cases, the network structure prescribes which players shall contribute to the value (or cost) of a given coalition, by bringing together their individual values.
The first part of the thesis is devoted to the introduction of a game-theoretical model that encompasses all the aforementioned classes of coalitional games. We introduce the class of *Generalized Additive Games* (GAGs), where the worth of a coalition is evaluated by means of an interaction filter, that is a map which returns the valuable players involved in the cooperation among players in the coalition.
The objective of this model is to provide a general framework for describing several classes of games studied in the literature on coalitional games, and particularly on graph games, and to give a kind of taxonomy of coalitional games that are ascribable to this notion of additivity over individual values. The general definition of the coalitional map allows various and wide classes of games to be embraced, as for example the simple games. Moreover, by making further hypothesis, our approach enables to classify existing games based on the properties of the coalitional map.
In particular, we introduce the class of *basic GAGs*, which is characterized by the fact that the valuable players in a coalition are selected on the basis of the presence, within the coalition of their *friends* and *enemies*, that is, a player contributes to the value of a coalition if and only if it contains at least one of his friends and none of his enemies is present. Several of the aforementioned classes of games can be described as basic GAGs, as well as games deriving from real-world situations. As an example, this model turns out to be suitable for representing an online social network, where friends and enemies of the web users are determined by their social profiles.
The interest of this classification is not only taxonomical, since it also allows to study the properties of solutions for classes of games known from the literature and provides some potentially useful tools for computing solutions of new classes of games that may fall into this classification. Indeed, some properties and solutions of such class of games are studied, with the objective of providing useful tools for the analysis of known classes of games, as well as for the construction of new classes of games with interesting properties from a theoretic point of view.
The second part of the thesis presents two approaches using our model to real-world problems described by graph games, in the fields of Argumentation Theory and Biomedicine.
The first application is to the field of Argumentation Theory, which aims at formalizing decision systems and associated decision making processes. One of its objectives is the search for sets of accepted conclusions in an argumentation framework, which is modelled as a directed graph where nodes represent arguments, i.e. statements or series of statements, and direct edges represent attack relations, which express conflict between pairs of arguments.
We focus on the *controversiality* of arguments, where the most controversial arguments are those for which taking a decision on whether they are acceptable or not is difficult, and we introduce a game-theoretical index based on the model of basic GAGs that measures the controversiality of arguments as the contribution of each argument to the conflict within the argumentation framework.
Considering persuasion scenarios, we argue that our conflict-based ranking may drive agents to select those arguments that should be further developed in order to strengthen a certain position in a debate, hence providing an index which measures the potential for development of arguments.
Lastly, we present a real-world application of the model of GAGs to the field of Biomedicine, and in particular to the problem of assessing the relevance of genes in a biological network. Among biological networks, *gene regulatory networks* are of great interest in the field of molecular biology and epidemiology to better understand the interaction mechanisms between genes, proteins and other molecules within a cell and under certain biological condition of interest. A crucial point in the analysis of genes' interaction is the formulation of appropriate measures of the role played by each gene to influence the very complex system of genes' relationships in a network.
With this objective, recently several centrality measures based on coalitional game theory have been successfully applied to different kinds of biological networks, such as brain networks, metabolic networks and gene networks.
We propose an approach, using basic GAGs, to the problem of identifying relevant genes in a gene network. An experimental study is conducted on a gene expression dataset from microarrays, related to a lung cancer disease, as well as a comparison with classical centrality indices.

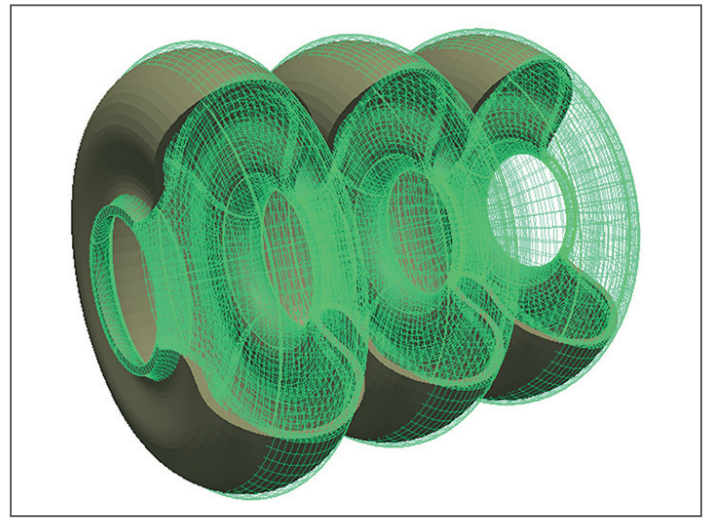
QUANTIFICATION OF THE IMPACT OF GEOMETRICAL VARIATIONS ON PARTICLE ACCELERATORS USING ISOGEOMETRIC ANALYSIS

Corno Jacopo – Supervisor: Prof. Dr. Carlo De Falco

The geometrical design of electromagnetic devices such as, for example, energy transducers, magnetrons, waveguides, antennas and linear accelerators is crucial in determining the device performance. In particular, for linear accelerator cavities, controlling the resonant frequency of the eigenmodes is important in order to guarantee the synchronization of the electromagnetic field and of the particle beam, which in turn determines the accelerating efficiency of the device.
Mechanical deformations cause a non-negligible frequency shift. This can be due to manufacturing imperfections or to the electromagnetic field itself (Lorentz detuning). The electromagnetic field excited in the cavity generates a pressure on the cavity walls that causes a small deformation. The change of the domain geometry gives rise to a shift of the frequencies of the resonant eigenmodes within. The variations to the eigenfunctions can also be responsible for undesired effects on the particle beam.
Isogeometric Analysis (IGA) was born in 2005, with the goal of *bridging the gap between Computer Aided Design* (CAD) and Finit e Element Method (FEM). The main distinctive feature of IGA is that CAD geometries, commonly defined in terms of Non-Uniform Rational B-Splines (NURBS), are represented exactly throughout the analysis, regardless of the level of mesh refinement.
Due to its strong relation to CAD, Isogeometric Analysis has already become a powerful tool particularly in the context of structural mechanics. A second advantage, when solving mechanical problems, is that an isoparametric approach can be adopted so that the computed (discrete) displacement is defined in terms of the same NURBS basis that defines the geometry and therefore the domain deformation is treated in a straightforward way, without loss of accuracy.
For solving Maxwell's equations, on the other hand, it has been proven preferable to abandon the isoparametric approach in favour of a choice of the solution space comprised of (push-forwards of) suitable B-Spline functions which guarantees an H(curl) conforming, and therefore spectrally accurate, approximation of the field. This choice, introduced by Buffa et al. (2010), leads to a discretization scheme which generalizes the classical Nédélec Finite Element Method and leads to solution spaces with higher regularity properties. It has been shown that IGA discretization methods can produce a highly accurate solution to the coupled electromagnetic-mechanic problem.
The main interest of this thesis work is the study of linear accelerator superconducting radio frequency cavities, such as the 9-cell TESLA cavity (Fig. 1), the evaluation of the Lorentz detuning effect and the evaluation of eigenmodes sensitivities with respect to geometrical changes. Geometrically accurate simulation methods, such as IGA, can be exploited to quantify the impact of uncertainties in the geometry via stochastic and deterministic approaches like Monte Carlo methods and Generalized Polynomial Chaos, in order to obtain statistical moments (mean value, variance, etc...) of our quantity of interest. Both approaches require the repeated solution of Maxwell's eigenvalue problem at collocation points, i.e., for cavities with perturbed geometry. To ensure consistency of the solution among the various eigenvalue problems and numerical efficiency, an eigenvalue tracking technique is proposed that is based on homotopies between collocation points and a Newton-like eigenvalue solver. The approach can be efficiently parallelized while tracking the eigenpairs.
Furthermore, to overcome the complexity of single simulations, we propose a general framework for domain decomposition techniques as a promising tool for reducing the computational time of linear accelerator simulation by exploiting the modularity of the computational domain.
In particular, we present two instances of methods fitting into this framework. The first one is inspired by the State Space Concatenation method recently introduced by Flisgen et al., while the second one is a Mortar method that exploits the inherent properties of the Isogeometric basis to naturally define the approximation space for the multipliers. Both approaches are cast in the general framework of the three fields method introduced by Brezzi et al. (1994). The application of these domain decomposition methods generates a substructuring procedure that can exploit the typical modularity of the accelerator structures to speed up matrix construction and memory consumption. Furthermore, it allows for the coupling of different grids and/or finite dimensional spaces in different sub-domains.
The thesis presents validation examples for the methods proposed and their application to the TESLA cavity case. Measurement data for the cavity deformations were provided by the Deutsches Elektronen-Synchrotron (DESY) facility in Hamburg.



2D cut of the 3D computational domain for simulating the 9-cell TESLA cavity and labels for the domains and the boundaries (yz section). The full cell is the result of a revolution around the z axis.



Deformation of a TESLA cavity under Lorentz detuning. The design cavity (in grey) is deformed by the electromagnetic pressure. The eigenmodes of the deformed cavity (in green) are shifted with respect to the starting configuration.

INTEGER COMPOSITIONS AND DNA SELF-ASSEMBLY STRATEGIES: A COMBINATORIAL AND A GEOMETRIC APPROACH

Ferrari Margherita Maria – Supervisor: Prof. Norma Zagaglia

It is known that some sequences of four elements, that are the nitrogenous bases A, C, G, T (namely adenine, cytosine, guanine and thymine) from which DNA is assembled, are repeated in the human genome many times. Because of the structure of DNA, different sequences that are equivalent up to cyclic rotation and reverse complementation, determine the same repeated pattern. In 1993, Bell et al. derived a formula for the number of equivalence classes of primitive patterns of DNA sequences of length n using the bijective correspondence between words on two letters of length 2n and words on four letters of length n. A further derivation of the formula for the classification of DNA sequences of length n was provided in 1997 by Chen and Louck using properties of cycle structures related to fixed points of the hypercube Qn.
In this thesis we propose a new approach to study properties of cyclic binary strings of length n, namely binary necklaces.
We start from the definition of composition of a positive integer n, which is an ordered sequence of positive integers whose sum is equal to n, and we consider two compositions to be equivalent if one can be obtained from the other by a suitable cyclic rotation of its elements, called parts of the composition. Let Wn be the set of the equivalence classes of compositions of a positive integer n under rotation, called cyclic compositions of n. The partition graph of n, Pn, is the graph having W'n:=Wn\{(11...1)} as set of vertices, where two vertices are adjacent when exactly one part of one vertex is the sum of two cyclically consecutive parts of the other one. The graph Pn turns out to be isomorphic to the Hasse diagram of the necklace poset without the vertices 00...0 and 11...1.
We investigate structural properties of the partition graph of a positive integer n; in particular we determine results about the minimum and the maximum degree of its vertices and we characterize some cyclic compositions of n having degree less than the maximum one.
We also study certain aperiodic vertices of Pn, called strongly singular, that can be used to build a 2n-cycle of Qn. We further examine a possible relation among certain cycles of Pn and Qn : to every cycle of Pn having aperiodic vertices we associate a suitable cycle or a set of disjoint cycles of equal length of Qn. Particular attention is given to cycles of the middle levels subgraph of Pn and Qn for n odd.

The second part of this work deals with techniques that use the Watson-Crick complementarity properties of DNA strands to self-assembly nanostructures, particularly polyhedra. For all of these methods, an essential step is designing the component molecular building blocks; thus there is an increased necessity for a mathematical approach to these design strategy problems. In this thesis we focus our attention on two different techniques: rigid tiling and the DNA origami method.
Rigid tiling is the self-assembly of nanostructures from rigid tiles, which are the branched junction molecule building blocks for tile-based DNA self-assembly. A tile type is a specification of the geometric structure and cohesive end complementarity of a rigid tile. We use the term bond-edge type for the type of connection between two cohesive ends with complementary DNA sequences. The design objective for rigid tiling is to minimize the number of different tile and bond-edge types needed to self-assemble a target construct without any incidental assembly of smaller constructs. One of the most significant mathematical design challenges for rigid tiling is modeling the tiles themselves. Because the arms are rigid, each cohesive end has a specific geometric orientation with respect to the tile, so that the attachment of two arms fixes the relative positions of the two tiles involved. To capture this geometric constraint, we adapt woodworking techniques, in particular half-lap splice joints, to model rigid tiles. This gives a concrete mathematical formalism and general scheme for developing design strategies for rigid tiling.
Using the half-lap framework, we show that the minimum number of tile types for 3-regular Platonic and Archimedean polyhedral skeletons is two, and with one bond-edge type needed for the 3-regular Platonic solids. In addition to the half-lap framework being useful in determining optimal design strategies, the formalism also exposes the significant design challenges inherent in creating assembly strategies that minimize tile and bond-edge types and maximize symmetry while preventing misassembly.
The DNA origami method makes use of one long single strand of DNA, called the scaffolding strand, and various short helper strands, called staple strands, to assemble the target structure.
In this process, the scaffolding strand traces the construct exactly once, and then the staple strands bond to the longer strand to lock it in the desired position. This means that to build a structure using the origami method, it is necessary to find a route for the scaffolding strand through the target structure. Because the scaffolding strand is usually circular, the route must end where it begins.
Since our goal is to construct polyhedral skeletons rather than filled, solid structures, we aim to find an Eulerian circuit, a closed walk that traverses each edge exactly once, as route for the longer strand through the structure. Such a circuit is called a threading for the construct.
If the graph contains vertices of odd degree, then augmenting edges must be added to make all the vertices of even degree. New angles other than those originally prescribed by the edges must be created in this circuit as the augmenting edges split the polygonal faces of our graphs.
We use this technique to efficiently construct Platonic and Archimedean 3-regular polyhedral skeletons by providing Eulerian circuits that leverage the inherent symmetries of the target constructs, so that maximum efficiency can be achieved.

DISCONTINUOUS GALERKIN SPECTRAL ELEMENT METHODS FOR THE ELASTODYNAMICS EQUATION ON HYBRID HEXAHEDRAL-TETRAHEDRAL GRIDS

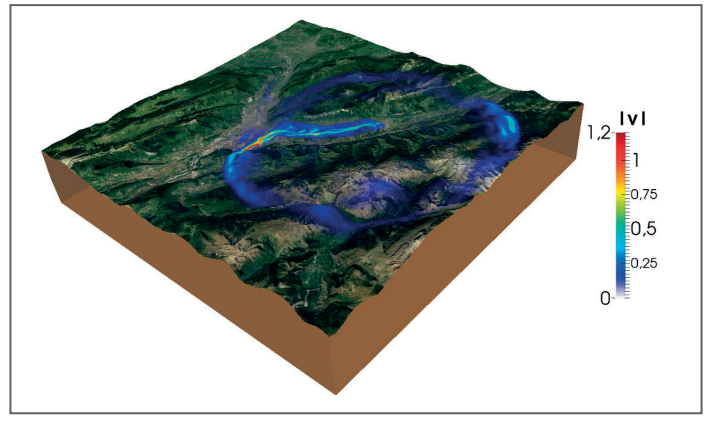
Ferroni Alberto – Supervisors: Prof. Alfio Quarteroni, Prof. Paola Francesca Antonietti, Co-Advisor: Dr. Ilario Mazzieri

In the last decades, the scientific research on elastic waves propagation problems, modelled through the (linear) elastodynamics equation, has experienced a constantly increasing interest in the mathematical, geophysical and engineering communities. In particular, the use of deterministic numerical simulations has been recognized to be a powerful tool to study the ground motion induced by large earthquakes on regions of intense seismic activity. Although earthquakes cannot be deterministically predicted, these analyses can play a crucial role to delineate effective strategies to mitigate as much as possible the risks related to earthquake effects for both human beings and infrastructures. The major challenges related to earthquake simulations are given by the need of geometric flexibility and accuracy. Geometric flexibility is required since in real applications the domain usually contains geological features characterized by complicated geometrical shapes and heterogeneities. Additionally, to precisely describe the effects of a seismic event it is essential to have an accurate approximation of the wave field from the source to the site.

Therefore, numerical methods must be able to limit dissipative and dispersive behaviours. Real earthquakes models are typically used on domains whose dimension, ranging from hundreds to thousands square kilometres, is very large if compared with the wave lengths of interest. This leads to a discrete problem featuring millions of unknowns. As a consequence, parallel algorithms must be designed in order to efficiently exploit high performance computers, especially for real case scenarios. Several discretization techniques have been developed for the approximation of the mathematical model based on the elastodynamics equation, such as the finite difference, the spectral element (SE) and the discontinuous Galerkin (DG) methods. Nowadays, thanks to their accuracy, flexibility and effciency, SE methods are probably the most successful tool in computational seismology, in particular for large scale applications.
In this thesis we consider the combination of SE techniques, that provide low dispersion and dissipation effects, with the flexibility of DG approximation, that allows to suitably tailor the grid size and the polynomial degree to the region of interest.
SE methods are historically based on discretizations made by tensor product elements (i.e., quadrilateral elements in 2D and hexahedral elements in 3D). However, generating hexahedral grids for complex geometries may require a huge computational and human effort. Indeed, automatic mesh procedures with hexahedral element are not able to accurately reproduce complex interfaces between different layers, especially when small angles are involved. The issues concerning the grid generation can be overtaken by using tetrahedral meshes. Indeed, different commercial or non-commercial softwares are available for the automatic generation of 3D unstructured tetrahedral grids, able to deal with very complex domains.
To exploit this flexibility in the meshing process, high-order or spectral element methods have been extended to tetrahedral elements by using either a nodal or a modal approximations. However, when an explicit time integration scheme is considered, SE formulations on tetrahedra can lead to huge efficiency losses, since they involve the inversion of a non diagonal mass matrix at each time step.

For these reasons, in this work, a DGSE approach on non-conforming hybrid grids is proposed, where the DG paradigm is not applied element-wise but at the interface between suitable macroregions..
On one hand, tetrahedral elements are employed only in those regions where we have complex geometries in order to drastically simplify the process of mesh generation. On the other hand, to fully exploit their efficiency, hexahedral elements are used in the remaining portions of the computational domain. Finally, since a crucial aspect of numerical methods for waves propagation is their capacity to limit dispersive and dissipative effects affecting the discrete solution, we provide a comprehensive dispersion and dissipation analysis of the three dimensional version of continuous and discontinuous spectral element methods on both hexahedral and tetrahedral grids.

The proposed method has been implemented into the SPEED software (http://speed.mox.polimi.it/).
SPEED is an open source parallel code designed with the aim of simulating large-scale seismic events in three-dimensional complex media. The main features of SPEED are presented and our code is validated on some benchmark test cases. Then, we apply our hybrid approach to realistic geophysical applications. In particular, we study the propagation of a plane wave in an elastic cavity as well as a soil-structure interaction problem between a railway bridge and its surrounding region.
Finally we simulate the seismic response of the Grenoble Valley in France, see **Figure 1**.



1. Grenoble valley test case. Snapshots of the magnitude of the computed velocity field (expressed in m/s)

NUMERICAL MODELING OF HYDRO-MECHANICAL COUPLING IN DEFORMABLE POROUS MEDIA: COMPACTION AND FRACTURES

Giovanardi Bianca – Supervisor: Prof. Luca Formaggia

Co-Advisor: Dr. Anna Scotti

Numerical simulations have become a fundamental tool to support and complete geological analysis in many applications. In the field of energy production, numerical simulations have been used for decades to track hydrocarbons from their generation to their migration and accumulation in reservoirs, hence reducing the risk in oil and gas exploration and enhancing production. More recently, with the development of novel renewable energies, mathematical models continue to provide a unique tool. In the design of systems for the extraction of geothermal energy high fidelity simulations of underground flows can give an insight into the mechanisms by which the injection of cold water triggers existing fractures in the rock, improving permeability and allowing water to flow through, be heated and be extracted to drive steam turbines and generate electricity. Another recent challenge is that of determining the safety of long-term storage of atmospheric carbon dioxide in subsurface saline aquifers or reservoirs, a.k.a. CO_2 sequestration. Indeed, the injection of a reactive substance in the underground results in chemical disequilibration and initiation of various chemical reactions. Moreover, as dissolved CO_2 comes into contact with rocks, it lowers the pH and triggers redistribution of carbonate aqueous species following a set of chemical reactions. Finally, numerical simulations can help in monitoring the behavior of contaminant substances in the underground flows and predict the generation of acidic waters in response to injection of industrial waste.

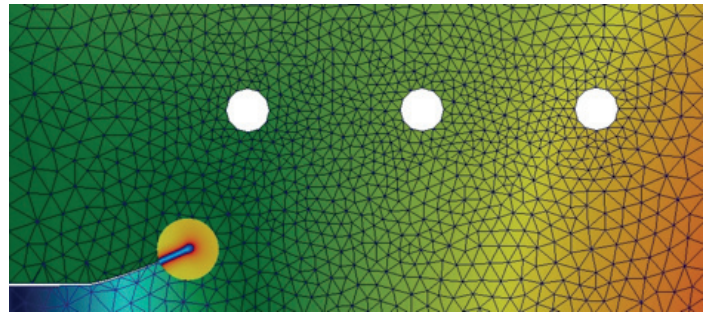
Any modeling attempt of these phenomena should account for complex coupling processes between the porous rock and the fluid that flows inside the pores. The hydro-mechanical coupling may arise from many mechanisms. The rock compaction, due to its progressive burial in the sedimentation process, causes an increase of pore pressure, which drives underground flows. The fluids inside the rocks are able to transport chemical species, which can react with each other and with the mineral present in the rock. Chemical reactions that involve solid-fluid conversions affect the rock properties in terms of porosity and permeability. On the other hand, the increase of fluid pressure in the regions where rock permeability is low counteracts the compaction process.

Furthermore, some of the above mentioned phenomena, such as the injection of high pressure fluid in the rock to improve permeability and enhance oil and gas production or geothermal heat recovery, may cause the artificial creation of fractures, which act as a preferential path for the fluid flow. Fractures can also originate spontaneously, as a consequence of the extremely large stresses. Being the crack opening related to the amount of fluid that can flow in the crack, the coupling between the rock and the fluid is very strong. The aim of this thesis is the study of underground flows with a particular insight into the coupling processes above described.

The first part of the thesis is focused on the interaction between a flow that transports a reactive specie and the rock. We propose a model to simulate the hydro-mechanical coupling in the presence of chemical reactions, and we develop an original numerical strategy to implement the complex nonlinear system obtained. Even though we consider a simplified case in which only one reactant is present and one type of reaction occurs, which may bring the reactive specie from the rock to the fluid, and vice versa, the numerical framework presented is rather general and features the key mechanisms that characterize both generation and migration of hydrocarbons, and of CO_2 sequestration. Equations that model chemical reactions may present discontinuities in the reaction rate, related to the availability of a specific reactant specie. An original aspect of the work consists in the application of a numerical technique that was originally developed to simulate the dynamics of a set of ordinary differential equations with discontinuous right hand side to a complex partial differential equation describing the concentration of the reactive specie in water.

The second part of the work is concerned with the propagation of fractures. First, we focus on the problem of crack propagation in a brittle elastic rock, driven from an external load, without modeling any poroelastic effect. The well known extended finite elements method (XFEM) is very suitable for the efficient simulation of rock displacement in case of a non-propagating crack. Having obtained the displacement solution for a fixed crack, crack propagation follows as a post processing from the evaluation of some experimental-based criteria. An alternative method to XFEM, very popular in the most recent literature, considers the crack as a smeared entity and provides a reformulation of the problem of crack propagation in terms of energy minimization. This method, based on a phase field model of fracture, incorporates crack evolution in the equations, at the price of a high computational cost. We propose a novel method, which we called Xfield, to simulate crack propagation in a brittle elastic material. The Xfield is developed with the aim of reducing the computational cost necessary to describe the crack as a smeared entity, and hence to model propagation with a sound energy-based criterion. The method combines a sharp and a smeared description of the crack, and inherits some aspects both from phase field models and from the extended finite elements discretization of the elasticity equation. Indeed, a large-scale displacement solution is obtained with the XFEM, while propagation is governed by the solution of a local phase field problem at the tip scale.

The last part of the thesis deals with the simulation of fracture propagation driven by the injection of a high-pressure fluid. This part was developed in collaboration with Prof. Raul Radovitzky and his group at the Massachusetts Institute of Technology under the one-semester exchange program ***Progetto Rocca*** sponsored by the ***Fondazione Fratelli Agostino ed Enrico Rocca***. We outline a novel numerical model for the simulation of hydraulic fracture, accounting for poroelasticity, based on a hybrid dimensional description of the fluid flow inside the crack and in the surrounding porous medium. The Xfield method developed in this thesis is then applied in this more complex framework.



Caption of Figure 1. The displacement of a specimen subject to an asymmetric notched three point bending test. The propagation of the crack is achieved with the Xfield method. At the crack tip, the local phase field solution, which drives the propagation, is overlapped to the displacement solution.

MINING LARGE ADMINISTRATIVE DATABASES: EFFICIENT AND SCALABLE ALGORITHMS FOR STATISTICAL MODELING

Grossetti Francesco – Supervisor: Prof. Anna Maria Paganoni

Healthcare administrative databases are becoming more and more important and reliable sources of clinical and epidemiological information. The present work marks the first Italian attempt which focuses on the acquisition, management and study of several data sources in the form of administrative databases regarding the Heart Failure pathology. All the data used in this thesis have been extracted from the administrative data warehouse of Lombardy Region, a region located in the northern part of Italy whose capital is Milan. One of the main goal of the present work is to identify, extrapolate and build a unique and consistent data structure to be used for statistical and research purposes. The administrative databases are conceived as repositories which are able to store many information but typically for managerial aims. This work is a step forward in moving the focus from a descriptive stand point of view to an inferential one. To achieve this goal, a great effort has been dedicated to the development of efficient algorithms, some of them have been finalized into a R package called msmtools. Moreover, this work studies the hospital admission-readmission process in order to explore the Heart Failure patient's epidemiology and to profile the health service utilization over time. We also investigate variations in patient care according to geographic area, socio-demographic characteristics as well as other administrative and clinical variables. The heterogeneity of the different data sources is fundamental to better characterize the disease progression and to possibly identify what are the main determinants of a hospital admission, readmission and death in patients with Heart Failure.

THREE ESSAYS IN MATHEMATICAL FINANCE
THIS THESIS COVERS THREE DIFFERENT TOPICS IN THE WIDE AREA OF MATHEMATICAL FINANCE

La Bua Gaetano – Supervisor: Prof. Daniele Marazzina

Part 1 deals with the application of matrix-variate Wishart processes in derivatives pricing.
Chapter 1 is devoted to the study of existing Wishart-based Stochastic Volatility models. The introduction of this kind of process in finance is motivated by the need to describe the multidimensional structure of asset variances. There are, indeed, empirical evidences that the dynamics of the implied volatility surface is driven by several factors. This causes the standard one-factor stochastic volatility models not to be flexible enough to consistently price plain vanilla options and forward volatility sensitive derivatives (e.g. forward starting and cliquet options). It is well accepted that a multi-factor approach would be necessary to take into account the variability of the skew. Further, the pricing of derivatives written on more than a single underlying assets requires a sound modelling of the multivariate dependence structure. A large part of existing literature considered vector-valued stochastic processes to model the multidimensional stochastic evolution of asset(s) volatility. The choice of Rd as state space for the volatility process, however, could lead to unsatisfactory dependence structures among variance factors. This is particularly true if we restrict ourselves to the case of affine processes.
In the light of the above, it appears reasonable to consider more general multidimensional processes: recently an increasing attention has been devoted to applications of matrix-defined stochastic processes in derivatives pricing. In particular, stochastic processes defined on the cone of real positive semidefinite matrices can be seen as natural candidates to model the latent volatility factors. In our analysis we focus on the so-called Wishart processes introduced in literature as a matrix generalization of square-root processes. A remarkable feature is that the analyticaltractability is fully preserved since these processes belong to the class of affine processes. Given the strict connection with the well-known CIR processes, Wishart processes have been used to define multi-factor and multi-asset extensions of the classic Heston model.
Despite the analytical tractability, the implementation of Wishart-based stochastic volatility models poses non-trivial challenges from a numerical point of view. Firstly, we discuss the models calibration and, exploiting the distributional properties ofWishart process, we propose efficient model approximations that alleviate the associated computational burden. Further we highlight the constraints that need to be satisfied in order to get a well-defined Wishart process and their impact on pricing performances. Secondly, we present simple and efficient simulation schemes for the asset price trajectories that allow to price path-dependent derivatives.
Chapter 2 presents a new class of pricing models that extend the application of Wishart processes to the so-called Stochastic Local Volatility (or hybrid) pricing paradigm. This is a very recent approach that is meant to combine the advantages of Local and Stochastic Volatility models. Despite the growing interest on the topic, however, it seems that no particular attention has been paid to the use of multidimensional specifications for the Stochastic Volatility component. Our work tries to fill the gap: we introduce two hybrid models in which the stochastic volatility dynamics is described by means of a Wishart process. The proposed parametrizations not only preserve the desirable features of existing Wishart-based models but significantly enhance the ability of reproducing market prices of vanilla options.
Part 2, based on a research project conducted with Professor Roberto Baviera (Politecnico di Milano) and Paolo Pellicioli, is concerned with the computation of CVA (Credit Valuation Adjustment) in the presence of Wrong Way Risk. CVA can be defined as the adjustment to be made to the price of a derivative transaction in order to reflect the inherent counterparty credit risk and, since the 2007 financial crisis, it has become one of the most relevant topic in the risk management industry. Departing from the assumption of independence between derivatives exposure and counterparty default probabilities leads to an additional source of risk (Wrong Way Risk) that requires a sound modelling of the dependence structure among market risk factors and default probabilities. Hull-White approach to Wrong Way Risk in the computation of CVA is considered the most straightforward generalization of the standard Basel approach. The model is financially intuitive and it can be implemented by a slight modification of existing algorithms for CVA calculation. However, path dependency in the key quantities has non elementary consequences in the calibration of model parameters. We propose a simple and fast approach for computing these quantities via a recursion formula. In the first part of Chapter 3 we show the calibration methodology on market data and CVA computations in two relevant cases: a FX forward and an interest rate swap. In the second part of the Chapter, we show that the proposed methodology leads to a straightforward application of Hull-White model to the computation of CVA for portfolios of derivatives with early termination features, such as American or Bermuda options. Extensive numerical results highlight the non trivial impact of early exercise on CVA.
Part 3, based on a research project conducted with Professors Emilio Barucci and Daniele Marazzina (Politecnico di Milano), is devoted to the study of the impact of relative performance based salary schemes on the risk taking incentives of asset managers.
In particular, in Chapter 4 we analyze the asset management problem when the manager is remunerated through a scheme based on the performance of the fund with respect to a benchmark. We show that it is not the asymmetric- fulcrum type feature that makes the difference in preventing excessive risk taking in case of a poor performance.
To prevent gambling when the performance deteriorates, it is important not to provide a fixed fee to the asset manager: remuneration should be sensitive to a very poor relative performance as in the case of a capital stake or of a management fee with flow funds. We provide empirical evidence on the mutual fund industry showing excessive risk taking in case of a very poor performance and limited risk taking in case of overperformance with respect to the benchmark. These results agree with a remuneration scheme including a fixed fee and a cap.

MATHEMATICAL AND NUMERICAL MODELING OF BLOOD FLOW AND SOLUTE TRANSPORT IN MICROVASCULAR DISTRICTS

Malgaroli Francesca – Supervisor: Prof. Paola Causin

Co-Supervisor: Prof. Riccardo Sacco

Microcirculatory districts, comprising thousands of vessels with diameter smaller than 200 microns, are the main actors in the distribution of blood flow and nutrients (oxygen, in a first place) to individual body organs. This process is highly complex, since the amount of blood and metabolites required by a certain tissue can greatly vary under different conditions. Up–to–date medical imaging techniques allow to study in a non–invasive manner regional blood flow in internal organs of human patients. The information content of such measurements is, however, far to be complete or fully understood, both in baseline conditions as well as in altered/pathological conditions.
Theoretical and computational approaches may help to increase the understanding of this complex scenario. Typically, mathematical models of microcirculation use lumped representations where vessels with similar diameter are compartimentalized in a unique class. This approach maintains a low number of unknowns and allows to explore in a simple and effective manner different regulatory mechanisms via phenomenological relations. However, the spatial distribution of field variables is lost, so that relevant geometrical and physical heterogeneities of the network cannot be represented, as well as complex internal and external interactions.
The aim of this thesis is to propose mathematical and computational models tailored to describe the physiological and mechanical behavior of large microcirculatory districts retaining spatial dependence of variables. We study appropriate numerical techniques to deal with the resulting coupled system of partial differential equations and we carry out numerical simulations on realistic microcirculatory districts. In particular, we apply the model to the study of the eye retina microcirculation, which features peculiar anatomical characteristics and exhibits a tight balance between nutrient supply and metabolic request.
The thesis is divided into two main parts. The first part is devoted to the mathematical modeling of large microcirculatory systems described as graph networks of distensible tubes. Numerical solution techniques and simulation results are presented at the end of each chapter. The simulations carried out using the proposed models show interesting local features of the network response, which are pretty different from what should be expected on the basis of experiments on isolated vessels and of theoretical studies with lumped models. In Chapter 1, we give a brief overview on the microvascular structure and function. In Chapter 2, we describe the geometrical modelization of the circulatory network. In particular, we consider networks obtained in silico from fractal dichotomic relations where the vessel diameter and length at each bifurcation are determined by the following fractal relationships

$$D_f^n = D_{d_1}^m + D_{d_2}^m, \qquad L = 7.4D^{1.15}.$$

We also consider a completely unstructured network generated by diffusion limited processes.
In Chapter 3, first we discuss a mathematical model for blood transport in a network. Blood is represented as a mixture of two Newtonian incompressible fluids, plasma and red blood cells. The pressure, velocity and hematocrit fields of blood in the arteriolar/venular branches are described by 1D equations, obtained upon averaging the 3D Navier Stokes equations

$$\frac{\partial v_s}{\partial s} + \frac{1}{r}\frac{\partial (r v_r)}{\partial r} = 0,$$
$$\frac{\partial (v_s H_D)}{\partial s} + \frac{1}{r}\frac{\partial (r v_r H_D)}{\partial r} = 0,$$
$$\mu_b\left(\frac{\partial^2 v_s}{\partial r^2} + \frac{1}{r}\frac{\partial v_s}{\partial r}\right) - \frac{\partial p_b}{\partial s} = 0.$$

Second, we discuss a mathematical model for transport and delivery of solute, and in particular oxygen, by blood flow in the network. The oxygen content in the arteriolar/venular vessels is described by steady state 1D equations

$$A\frac{\partial \overline{J}_s}{\partial s} + 2\pi\alpha_c \mathcal{L}_p \overline{p}_c f_c(R) = -A\frac{\partial \overline{J}_w}{\partial s} + 2\pi\alpha_c \mathcal{L}_p \beta_t p_{t,w}(r f_c(r))\Big|_{r=R},$$

where the flux

$$\overline{J}_s = \overline{v}_s \omega_1(\alpha_c + C_{\mathrm{Hb}} H_D \widetilde{S}_{\mathrm{O_2}})\overline{p}_c - D_c \frac{\partial}{\partial s}\left(\overline{p}_c(\alpha_c + \frac{D_{\mathrm{Hb}}}{D_c} C_{\mathrm{Hb}} H_D \widetilde{S}_{\mathrm{O_2}})\right)$$

includes both the free and hemoglobin-bound fractions.
In Chapter 4, we discuss a mathematical model of blood transport in vessel networks with compliant walls. The pressure and velocity fields of blood in the arteriolar/venular vessels are described by 1D equations analogous to the one discussed in Chapter 2. However, in this case, the blood flow results to be dependent on a conductivity parameter, function of the area and shape of the tube cross section and the biophysical properties of blood itself, define as

$$\sigma = \frac{\widehat{R}^4}{\mu_b}\int_{A^*} v_s^* dA^*.$$

Both empirical (experimentally-derived) and theoretical models are used to describe the relationship between the cross section area and the pressure loads. When dealing with thin–walled venules, the possibility of section buckling is also considered. A mathematical model to recover the unloaded configuration is also discussed.
In Chapter 5, a simple model of autoregulation mechanisms is proposed on a single vessel, in which the vessel diameter is regulated by the concentration of oxygen and nitric oxide in the vessel wall. Nitric oxide is assumed to influence the level of calcium ions in the smooth muscle cells which, in turn, give rise to muscle contraction and thus diameter variation. A radial solution for solute transport along the vessel wall, described as a three–layered structure (endothelium, smooth muscle cells layer and tissue) is obtained using Bessel–type functions.
In the second part of the thesis, we consider a specific microcirculatory district, the eye retina circulation and we apply the mathematical and numerical models, developed in the first part, to its study. In Chapter 6, we give a brief overview of the anatomical feature of the eye retina. In Chapter 7, we couple the models discussed in the third chapter for the blood flow and oxygen transport along the network with a model for the oxygen transport in the retinal tissue. The model accounts for the three-dimensional anatomical structure of the eye retina. The model is validated against available experimental results to identify baseline conditions. Then, a sensitivity analysis is performed to assess the relevance of the variation of different parameters of clinical interest on a selected number of significant output variables. In Chapter 8, we focus our attention on the retinal tissue. We solve the following diffusion-reaction equation for solute transport and consumption with a Michaelis Menten term

$$-D_t \alpha_t \frac{\partial^2 p_t}{\partial z^2} = \mathcal{Q}(p_t, p_c)$$

by a semi-analytical technique which makes use of the so–called homotopy perturbation method. We perform a sensitivity analysis to theoretically weight out the relative contributions of various factors to the oxygen profile in the retinal tissue, in particular oxygen source terms and consumption rates. Eventually, in Chapter 9, we study transport of solutes with different characteristics (molecular weight, lipophilicity, . . .) along the complete posterior part of the eye, including sclera, choroid, retina and vitreous. This study is devoted to develop a pharmacokinetical mathematical model to assess drug levels subsequent to a trans–scleral drug implant. The domain is partitioned into different regions, each of them with characteristic physiological structure and function. The membranes limiting the different regions, which have fundamental importance since they represent physical obstacles to drug diffusion, are described by appropriate partition laws including permeability parameters and active transport effects. The filtration velocity is described according to the steady-state Darcy equation while the drug transport by a diffusion-reaction equation. In particular, the oxygen transport equation in the retina, described by a mixture of tissue and blood vessel phases, is:

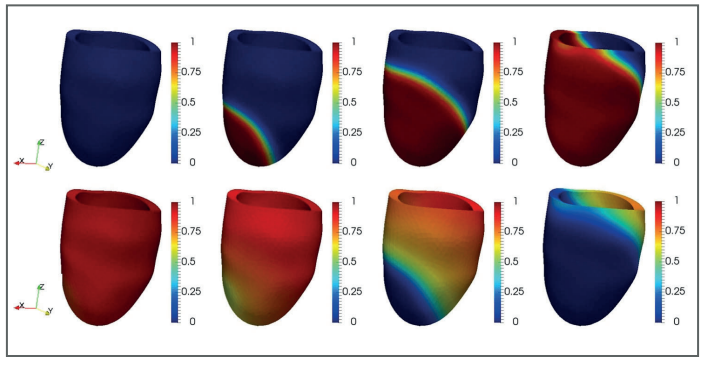
$$(1-\phi)\frac{\partial C_{Rt}}{\partial t} = (1-\phi)\left[D_R\frac{\partial^2 C_{Rt}}{\partial x^2} - (v_{Rt}+v_{act})\frac{\partial C_{Rt}}{\partial x} - k_{Rt}C_{Rt}\right] + \beta(C_{Rb}-C_{Rt}),$$
$$\phi\frac{dC_{Rb}}{dt} = S_{Rb}(t,x) - \beta(C_{Rb}-C_{Rt}) - \phi k_{Rb}C_{Rb}.$$

A theoretical analysis is carried out to establish lower and upper bounds for the drug in the retina as a function of the initial conditions, external sources and boundary conditions. The problem is then solved by the use of numerical techniques, establishing the drug profile as a function of time from drug implant. A sensitivity analysis is also carried out for different molecular properties.

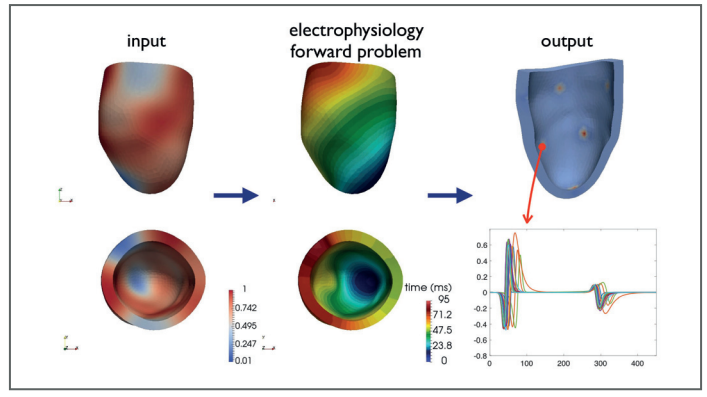
REDUCED-ORDERMODELS FOR INVERSE PROBLEMS AND UNCERTAINTY QUANTIFICATION IN CARDIAC ELECTROPHYSIOLOGY

Pagani Stefano – Supervisors: Prof. Alfio Quarteroni, Dr. Andrea Manzoni

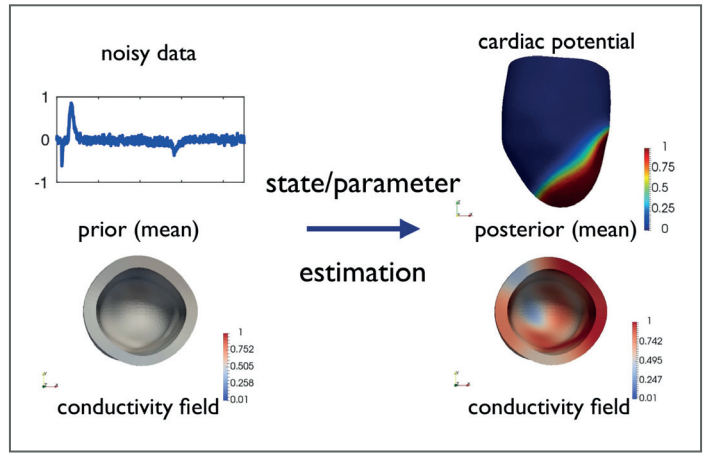
The objective of this Thesis is to develop reduced-order models (ROMs) for the efficient and accurate solution of uncertainty quantification (UQ) and inverse problems arising in cardiac electrophysiology. Cardiac models could be affected by a significant amount of uncertainties related to both physical and geometrical parameters, such as inter-subject and intra-subject variability. Developing UQ and inverse techniques is crucial for a personalization of these models: a notable example is the estimation of myocardial ischemia shape and location in a realistic left ventricle, which represents an important application proposed in this work.
Inverse and UQ problems involvemany queries to input-output maps requiring the solution of a nonlinear parametrized coupled system of ordinary and partial differential equations (PDEs), such as the monodomain equation equipped with ionic models. Prohibitive computational costs occur when full-order models (FOMs), relying e.g. on the finite element method, are adopted for the numerical approximation of the PDEs. In order to reduce the computational complexity, we exploit the reduced basis (RB) method to approximate the parametrized PDE solution, using the proper orthogonal decomposition technique for the basis functions construction and hyper-reduction techniques for the efficient evaluation of nonlinear terms.
However, applying state of the art RB method is not straightforward for this application, since the electric potential evolution is characterized by a sharp traveling front highly sensible to changes in the model parameters. In order to recover a rapid and reliable approximation, we develop localized-ROMs based on suitable clustering techniques for the sake of local RB spaces selection. Moreover, since classical error estimators are out of reach in this context, we introduce ad hoc statistical error surrogates for error quantification. This latter ingredient is essential for the solution of inverse problems in order to minimize the propagation of the approximation error, which could lead to biased estimates when a FOM is replaced with a ROM.
After providing a detailed analysis and a comparison of these techniques on some suitable numerical tests, we apply the proposed method for sensitivity analysis and uncertainty quantification.
In particular, we study how the model parameters affect the electrocardiogram or action-potential shape, providing interesting insights about the role and the importance of cardiacmodel parameters.
Furthermore, we consider filtering techniques for the solution of parameters estimation problems. We develop a reduced-basis state-parameter ensemble Kalman filter and we analyze its consistency and effectivity. This methodology is finally applied to the estimation of myocardial ischemia shape and location on a patient-specific left ventricle.



1. Cardiac potential evolution during a heartbeat



2. Input/output map on a subject-specific left ventricle



3. Inverse problem solution
using the reduced basis ensemble Kalman filter

FUNCTIONAL DATA ANALYSIS FOR HIGH DIMENSIONAL AND COMPLEX GENOMIC DATA

Parodi Alice Carla Luisa – Supervisor: Prof. Piercesare Secchi

The Chair of the Doctoral Program: Prof. Irene Maria Sabadini

In this work we aim to connect the statistical techniques of Functional Data Analysis with the high dimensional and complex setting of genomic data. Given the recent development of more and more advanced techniques to collect life-science data, the challenge is now the definition of efficient statistical tools to extract meaningful information from this huge amount of complex records. The research we present in this work deals with real applied problems, collected from the biological environment of the -omics community, providing advanced statistical techniques to efficiently analyze these data.
From early XX century, when the Genetic science was born, many innovations have been introduced: from Gregor Mendel and his heredity studies, we are now in the era of Next Generation Sequencing. This is a collection of methods and laboratory techniques to analyze the genome, the transcriptome and the epigenome to identify not only the sequence of nucleotides our DNA is made of, but also the complex mechanisms of codification of proteins and the complete nucleus environment where DNA is immersed in. However, these new techniques produce measurements, which could be intrinsically longitudinal, since they vary in time or space, or which could affect the phenotypic expression of individuals in different ways with the passage of time. Therefore, in this work, we introduce functional data techniques to consider the whole longitudinal structure of the data. Moreover, we ensure to deal with the computational effort required to analyze such a huge amount of data and to allow the reproducibility of the analyses in different datasets (both from the same kind of biological experiment and from different areas of investigations) developing efficient R packages, mainly coded in c++, and uploading them on public repositories.
The dissertation is split in two parts: in Part I the main focus is the isolation of phase and amplitude variability of a functional data set, while in Part II the main focus is the analysis of the influence of external factors on functional data.
In Part I we focus on the distinction of the two types of variability that curves can exhibit: amplitude variability associated to the magnitude of the signal of curves; phase variability associated to the timings of the features measured, ignoring their sizes. Two illustrative case studies, for which the distinction between these two types of variability is crucial, are presented.
In Chapter 1 a ChIP-sequencing experiment is presented: it consists of the isolation of a specific protein in the nucleus of the cells and in the analysis of its connection with the double helix of DNA. A coverage function is measured throughout the genome to quantify the connection between the DNA and the protein: for each basis of the genome a count is registered; the higher is the count, the stronger is the evidence for the connection with the protein in the specific locatio. Once the regions of the genome where the protein is present are isolated, we investigate on the possible differences in the linkage between DNA and protein, looking for differences in the shapes of the coverage profiles. This shape analysis can be led with a joint analysis of phase and amplitude variability and in this work we adapt the functional data technique of k-mean alignment to the specific case of ChIP-sequencing experiments. We apply this method to many ChIP-sequencing experiments, mainly related to the oncogene Myc, and we detect significant differences in shapes connected to differences in the location of peaks, in their association with up and down regulated genes and in the motif detection.
In Chapter 2, instead, we describe a dataset related to the study of the progression of Alzheimer's disease: the joint analysis of phase and amplitude variations in the longitudinal measure of the results of the Mini-Mental State Examination (MMSE) of patients is presented. This measurement quantifies the cognitive decline of patients and can be used to distinguish between faster and slower decliners. This distinction is reliable once a proper time-zero, or initial point, is defined for the disease. The classical definition of the time-zero as the time of the first visit, or a specific age of patients, seems to be unsatisfactory, leading us to define the Temporal Clustering, a new method which jointly analyzes phase and amplitude variability to detect both a time-zero for the initial expression of the disease for each patient and the type of decline: each patient is associated to a slower or faster decline cluster. This method is similar to the k-mean alignment, but uses a known parametric expression of the cognitive decline to represent the MMSE of patients. Once we have categorized each patient by his decline speed, we can detect whether some genomic markers, like SNPs, affect this categorization: for example, we show the relationship between a specific variant in the APOE gene and the faster decliners cluster.
Beside the internal source of variation of functions considered in Part I, in Part II we focus on the external influences that may affect functional data. Specifically, we investigate the influence of genomic features, like SNPs or microbiome, to the longitudinal growth or lung development of children, with the definition of a function-on-scalar linear model. To isolate the genomic measurements that really affect the functional outcome and estimate their effect, we develop a new method, called Functional Linear Adaptive Mixed Estimation – FLAME –, to deal with the high dimensional and the sparse setting of this function-on-scalar regression. We present the method with its theoretical properties and computational details and introduce two real case studies to prove its efficiency in the high dimensional setting.
In particular, in Chapter 3 we detail FLAME and its dual goal: the selection of the relevant predictors and the estimation of their influence controlling the smoothness structure of the fitted coefficients. Specifically, FLAME allows to embed the functional regression coefficients into a Hilbert Space that can be different from the space of the functional outcome. In particular, the Hilbert Space of the coefficients is a Reproducing Kernel Hilbert Space so that a proper choice of the kernel leads to control the regularity structure of the coefficients, as for example the smoothness level or the periodicity. FLAME is then used to identify the 12 relevant Single Nucleotide Polymorphisms, among the 10,000 introduced, which influence the lung development of children affected by asthma: one of these SNPs was not detected by other functional methods, but is associated to a gene that has already been related to the asthma disease.
Finally in Chapter 4 a further application of FLAME is presented: it deals with the influence of the stool and buccal microbiome on the growth of children and aims to detect the effects of the microbiome of young children on the obesity disease. Specifically, measurements of the abundances of bacteria at the genus level are collected and their influence on the growth of children in their first years of age is investigated: we isolate some bacteria from the Firmicutes and Bacteroidetes phyla that affect the ratio weight/height of children in their first two years of age.

NUMERICAL MODELLING AND SIMULATIONS OF NONLINEAR ELASTOPLASTICITY FOR GEODYNAMICS APPLICATIONS

Porcù Roberto – Advisor: Prof. Edie Miglio

The theory of plate tectonics describes the large-scale deformation of the Earth's lithosphere, which is broken up into seven major plates and several minor plates able to move relatively to each other. Due to this motion the major deformations, which concentrates along the boundaries of the plates, give rise to strong geological phenomena. Three main types of plate boundaries have been observed: convergent, divergent and transform boundaries.
Continental rifts are tectonic products which occur along divergent boundaries and consist of a localized lithosphere extension until a complete break. There are some important reasons motivating the investigation about these geodynamic processes, which are: continental rifts have a deep influence on the geographic distribution of a variety of natural resources such as geothermal energy, groundwater, mineral deposits and hydrocarbon reservoirs; furthermore, through volcanism and magmatic products, rifting provides information about the physical and chemical properties of the mantle; finally rifts can be the sources of natural hazards like earthquakes and volcanoes.

During the last decades researchers have been studying continental rifts by means of both laboratory experiments and numerical simulations. The former, called analog sandboxes, are constitued by boxes, usually made of plexyglass, containing coloured sand placed along horizontal superposed layers. When some parts of the external box are displaced the sand deforms. These experiments present several disadvantages such as the inevitable high simplification of the model, the impossibility to provide quantitative information about the internal state of the system and the impossibility to take into account the thermodynamic effects. The latter, called numerical sandboxes, are characterized by the generally accepted assumption of a purely linear continuum mechanics theory which is incoherent with the finite strain deformation regime that characterizes the nature of the problem at hand. Furthermore we observed that every numerical result found in the literature has been obtained by means of artifacts, the most common being the imposition of a seed of rheological weakness placed at the bottom of the computational domain. We are legitimated to suspect that these artifacts are necessary to force the system evolving in the desired way and to observe, in the deformed sandbox, the expected shear-bands pattern that otherwise would not have formed. In addition to this we observed a substantial disagreement between the results obtained by means of different commercial and/or non-commercial solvers. The aim of this thesis is the investigation and application of a different approach to the problem, characterized by the assumption of the purely nonlinear continuum mechanics theory, without recurring to any artifact. For this purpose a new C++ code has been developed for the numerical simulations of rift-like problems. Indeed the commercial and non-commercial softwares that have been used by several authors for the numerical solutions that they present in the literature, are inadequate for geodynamics applications for the following reasons: they implement a linear continuum mechanics theory that is incoherent with the finite stain deformations regime; they have been developed for particular applications and then they can not be adapted to different geometries and rheologies of the problem, such as stratified domains made of different overlapped layers.

Furthermore our code has been parallelized in order to reduce the computational cost. We believe that our purely nonlinear approach can provide the natural development of the shear-bands pattern that we expect to observe in the deformed configuration of the system. In this case our solution would represent a proof of the fact that the finite kinematics elastoplasticity theory is sufficient to explain the shear-bands formation. In our results we have observed what we were expecting, that is the natural development of the shear-bands patterns and the formation of the characteristic "horst-graben" structures which, as illustrated in the first chapter, are typical of continental rifts. This outcome is very important because confirms our initial belief that a purely nonlinear approach is the correct choice for the coherent modelling of geodynamics applications. Indeed this approach justifies the fact that finite kinematics elastoplasticity is sufficient to explain the shear-bands formation and that there is not the need for the artifacts found in the literature used to force the problem in the desired way.
Even though finite kinematics elastoplasticity is a well-developed theory, in this work we have presented our apported original contributions which describe some aspects of the theory that were still unexplored. In particular we provide the explicit and complete algorithmic tensorial formulation of the plastic exponential return map for the case of an uncoupled volumetric/deviatoric formulation of the problem applied to a three-fields weak variational formulation of the nonlinear elastoplastic problem. This approach was firstly introduced by J.C. Simo and is known as the mixed Jacobian-pressure formulation.
The reason that motivates the adoption of this formulation lies in the volumetric locking arisement whenever a nearly isochoric deformation is enforced point-wise via a low-order Galerkin finite element method. The volumetric locking consists in over-constrained pressure fields and, by consequence, overly stiff numerical solutions. The fundamental idea to circumvent the occurrence of this issue consists in the weak enforcement of the volumetric constraint by means of a new independent volume field variable together with its dual variable that plays the role of a Lagrangian multiplier and is interpreted as the Kirchhoff pressure.
In addition to this we derive the explicit definition of the exact elastoplastic tangent modulus, which is a product of the Newton-Raphson linearization of the problem, for any of the three possible cases which can arise depending on the number of different principal stretches.
Our code implements the purely nonlinear theory and is able to handle stratified geometries made of an arbitrary large number of overlapped layers, thus reproducing a real sandbox. Furthermore our program can accommodate any type of hyperelastic rheology and plastic yield criterion; indeed these new features can be inserted in the code by a simple implementation of the Helmoltz free energy functions and of the plastic yield functions which characterize the new rheologies. We tested our software on well-known benchmarks obtaining good results and observing a correct behavior of the global constitutive update algorithm: since this algorithm contains the implementation of our original contributions discussed above, then those results represent a proof of the consistence of the new concepts introduced in this work. In conclusion we have also verified that the parallelization based on the MPI paradigm provides a good performance speedup.
The results that we have obtained represent a strong motivation to further improve this work starting from the inclusion of the following extensions: first of all the improvement of the material constitutive properties by addition of the plastic hardening/softening behavior and of the complete nonlinear elastoviscoplastic rheology; in addition the implementation of mesh adaptivity; finally the extension of the model by inclusion of the thermodynamic effects.

ROBUST STATISTICAL METHODS IN FUNCTIONAL DATA ANALYSIS

Tarabelloni Nicholas – Advisor: Prof. Anna Maria Paganoni

This work explores the problem of drawing robust, statistical inference from real, complex functional data. This is a particular instance of the Big Data concept where high-dimensional observations are constituted by measurements of some quantity of interest that can be naturally indexed with respect to an independent variable, like time or space.
The recent research branch of Functional Data Analysis (FDA) has been steadily growing around the analysis of such data, thanks to the flexibility and wide applicability of the functional data model to a number of different phenomena, e.g. in environmental, economical, biomedical or engineering disciplines.
Due to the richness and complexity of functional data, a common problem to virtually any FDA application is the correct inspection and management of data variability. Although that, outlier detection and robust statistics are not yet a well-established practice in FDA. Considering that in this context inference typically relies on a small number of observations compared to their degrees of freedom, and thus datasets can become easily contaminated by noisy observations or unnatural variability, the need for proper robust techniques is pressing.
The objective of this work is to share some new contributions to this field, in terms of both new methods and tools, motivated by real applications. These contributions are based on some concepts from robust statistics for multivariate data that have been recently extended to the functional case, like statistical depths, multi-dimensional quantiles and robust estimators. We will show how such techniques can be used either for a safe exploration of functional datasets and identification of anomalous observations, or as flexible and meaningful building blocks for further inferential analyses.