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PhD Yearbook | 2019

PHD COURSE IN MATHEMATICAL MODELS AND METHODS IN ENGINEERING

Chair:
Prof. Irene M. Sabadini

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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SCALABLE ADAPTIVE SIMULATION OF ORGANIC THIN-FILM TRANSISTORS

Pasquale Claudio Africa - Advisor: Prof. Carlo De Falco

Organic semiconductors are outstanding candidates for becoming the material platform for a plethora of highly innovative electronic devices.

Several factors have motivated a continuous research in organic semiconductor technologies, such as easy and low-cost fabrication of large area circuits, mechanical flexibility, high transparency and bio-compatibility. Since such materials can be processed from solution, they can be formulated as functional inks and deposited by means of printing techniques adapted from graphical arts (ink-jet, screen printing, spray coating, flexography to cite but a few).

An important trend is that key industry sectors are implementing a variety of products based on organic and printed electronics. A strong engagement and product introduction is seen in the automotive, consumer electronics, packaging and medical/pharmaceutical sectors. New possibilities of application of this kind of technology, as shown in fig. 1, can be grouped into five clusters:

- lighting (OLED);
- light-harvesting (photovoltaics);
- flexible displays;
- electronics and components (memories, batteries, ...);
- integrated smart systems (smart objects, sensors and smart textiles).

The present research project focuses on mathematical models and numerical methods for the simulation of Organic Thin-Film Transistors (OTFTs), which are field-effect transistors produced by depositing thin films of an organic semiconductor layer over a non-conducting substrate, such as glass. OTFTs are extremely useful in applications such as flexible integrated circuits, sensors, organic memories, e-paper and RFID tags; moreover, they have turned out to be promising backplane drivers in OLED-based flexible displays. Recent advancements in organic material fabrication techniques directed the researchers to make use of flexible substrates, such as paper, plastic, glass and fiber, for low cost and light weight flexible applications.

The disordered morphology and energetic structure of organic semiconductor materials warrants for the development of suitable mathematical models and numerical methods for dealing with the peculiar properties of charge transport in OTFTs. Furthermore, the typically extreme form-factors of such devices constitute a challenge for numerical simulations which demands for an efficient implementation based on advanced High Performance Computing (HPC) techniques.

We develop a hierarchy of mathematical models based on partial differential equations to describe charge transport in OTFTs. The basis of such model hierarchy is the well known Drift-Diffusion system of equations suitably adapted and extended in order to account for physical phenomena, such as energy barrier lowering and charge injection at metal-semiconductor interfaces, and state-of-the-art constitutive relations that are representative of the molecular disorder of organic semiconductor materials. A particular attention has been devoted to ensure that the presented models provide a consistent representation of the simulated system under equilibrium, transient and time harmonic regimes of operation.

The models are firstly presented in a one-dimensional framework to derive a computationally efficient parameter estimation procedure used to characterize relevant physical properties of such materials. Then they are extended to 2D and 3D geometries in order to account in a more natural way for a set of inherently multi-dimensional phenomena such as the non-planarity of semiconductor-insulator interfaces due to the solution processing of the materials, parasitic capacitances due to coupling between metal layers, the bending of energy bands at the semiconductor-substrate interface away from contacts and the contact resistance due to current-crowding effects.

Robust numerical methods are required to simulate the above described models. We propose a one-dimensional numerical formulation based on a modification of the Scharfetter-Gummel discretization scheme that is thermodynamically consistent even in those cases where the classical Einstein relation between the mobility and the diffusivity coefficient does not hold. Then the formulation is extended to meshes of quadtrees (2D) and octrees (3D), that are hierarchical, non-conforming Cartesian grids, by developing a strictly monotone discretization scheme that guarantees non-negative and oscillation-free solutions for problems with steep boundary and interior layers. To increase the accuracy of the numerical scheme we construct difference formulas that enable to recover higher order approximations of the solution gradient and the solution itself: the recovered gradient and solution are exploited to build proper a posteriori error estimators to drive a metric-based mesh adaptation procedure. The advantages of the proposed approach in terms of efficiency with respect to a standard solve-mark-refine technique are discussed.

Finally, the properties of a set of robust linearization methods are investigated, with a special focus on those preserving the positivity of density variables throughout the simulation algorithm.

From an implementation perspective, recent progresses in data structures and algorithms for creating, hierarchically refining, balancing and partitioning meshes of quad- and oct-trees has brought this class of grids to the forefront of the research interests in the HPC community as a key tool for attaining extreme scalability. Achieving this goal drives the development of an efficient, parallel, scalable code. The implementation strategies followed in our code are examined and motivated.

Fig. 1 - Fields of applications of organic electronics. Source: "OE-A Roadmap of Organic and Printed Electronics 2015"

WAVELET TRANSFORM AND INSTANCE-BASED METHODS FOR NON-STATIONARY TIME SERIES ANALYSIS

Francesco Cannarile - Supervisor: Prof. Enrico Zio
Co-Advisor: Prof. Piero Barladi

In the Industry 4.0 era, an increasing quantity of time series data is collected from various real-world applications including, for example, healthcare, finance, weather forecasting, astronomy, manufacturing, reliability engineering. The motivation behind the present Ph.D. thesis work is Prognostics and Health Management (PHM) which is an interdisciplinary field of research and application aiming at detecting the degradation onset of industrial equipment, diagnosing its faults, predicting its Remaining Useful Life (RUL) and proactively managing its maintenance to improve system safety, availability and reliability. PHM requires monitoring a large number of equipment parameters to evaluate the health state of the equipment. The monitored parameters of practical interest are typically non-nonstationary time series, i.e., their statistical and frequency characteristics change with time. This is due to the fact that the monitored parameters are influenced by the environment in which the equipment operates, which is typically evolving as time passes, and by the equipment degradation which is an irreversible process which typically causes monotonic trends on the parameters. Another difficulty of PHM is that the information on the true equipment degradation level is not available in many applications due to the cost of its estimation. As consequence, the available data are incomplete, right-censored time series. These issues in PHM have motivated the development of time series analysis methods with following research objectives: development of an anomaly detection method for non-stationary time series; development of a classification scheme for non-stationary curves and development of a similarity-based regression method for time series prediction in presence of incomplete data. From a PHM perspective the three research objectives correspond to fault detection, fault diagnostics and fault prognostics, respectively. To achieve these objectives, we have considered wavelet and instance-based (also known as similarity-based) methods.

With respect to research objective , we have developed a novel method for sensor data validation based on the analysis of data regularity properties through the joint use of Continuous Wavelet Transform (CWT) and image analysis. Anomaly detection is performed by comparing the similarity between the CWT scalogram obtained from the test signal with those obtained from historical data in nominal condition with a fixed threshold. The developed method has been successfully applied to temperature signals from a reactor coolant pump. Differently from the typical sensor data validation methods which detect sensor malfunctions by observing variations in the relationships among measurements provided by different sensors, the proposed solution can be systematically applied to a fleet of plants, without requiring sensor grouping.

With respect to research objective , we have developed a novel Functional Data (FD) based Empirical Classification System (ECS) for diagnosing the degradation level of industrial equipment. The developed ECS combines wavelet smoothing, elastic registration and LASSO multinomial logistic regression. The proposed method has been successfully applied to case studies concerning solenoid valves mounted on train braking system and knives used in the packaging industry. The proposed solution which, at the best of our knowledge, is a novel approach in fault diagnostics, is shown to allow improving the classification performance with respect to traditional approaches of the PHM field.

Finally, with respect to research objective we have developed a novel direct RUL algorithm capable of exploiting the information provided by incomplete, right-censored degradation trajectories for effective RUL prediction and quantification of its uncertainty. The novel developed method combines similarity measure with Dempster-Shafer evidence theory. Its application to two case studies concerning turbofan engines and cutting tools used in the manufacturing, has shown that it provides more accurate RUL predictions in comparison with a similarity-based regression method of literature. Furthermore, the proposed method allows properly quantifying RUL predictions uncertainty.

The obtained results show that the developed time series methods can be effective in PHM industrial applications and can support the development of condition-based and predictive maintenance strategies.

STABILITY ANALYSIS IN SUSPENSION BRIDGES THROUGH SOME NEW MATHEMATICAL MODELS

Alessio Falocchi - Supervisor: Prof. Filippo Gazzola

The main object of study of this work is the mathematical modeling of suspension bridges. The motivations are multiple, first of all the fact that these structures manifested and manifests anomalous oscillations. Many observations throughout history have recorded that torsional instability afflicts suspension bridges, leading in some cases to the collapse of the structure. Although the remarkable progresses of the civil engineering in the nineteenth and twentieth centuries, the bridges also today collapse, manifesting problems often difficult to understand. The most famous case, here studied in deep, is the collapse of the Tacoma Narrows Bridge in 1940, in which a sudden change from vertical to torsional oscillations led to the failure. This event burst a spark in the scientific community that from the next years started to formulate hypothesis and theories on the incident. Currently there is not a unanimously accepted explanation about the origin of instability; there are many theories from vortex shedding to flutter, from structural instability to parametric resonance. For these reasons, suspension bridges raised interest not only in the engineering community, but also among mathematicians and physicists. Really, this fact is not surprising at all. Already two centuries ago, Navier studied the suspension bridges and published at the Imprimerie Royale of Paris "Mémoire sur les ponts suspendus" (1823), in which for the first time this topic is deepened through an analytical and abstract approach.
The main elements composing suspension bridges are four towers, a rectangular deck, two sustaining cables and some hangers. The hangers link the deck to the main cables, obtaining a structural configuration optimal to bear the weight of decks having long span. The setup of a reliable model for these structures appears quite demanding, because it has to be on the one hand simple enough to be mathematically tractable and on the other hand sufficiently accurate to describe the real bridge behavior. Our modeling choices are based on real observations, recorded by witnesses and instruments during the oscillations of some suspension bridges; on this purpose, Chapter 2 is devoted to the most interesting cases. We include not only the Tacoma, but also the Brighton Chain Piers, the Angers Suspension Bridge, the Broughton Suspension Bridge, until to the famous episode of the London Millennium Bridge in 2000.
In the thesis we present three new isolated models for suspension bridges aiming to show that the torsional instability arises suddenly due to the nonlinear configuration of the structures. The energy, given by the wind excitation, is introduced in the system through the initial conditions, avoiding to consider the wind as an explicit external force and dealing with the problem from a different point of view.
In general, we proceed writing the total energy of the system and deriving from variational principles two nonlinear partial differential equations in space and time. Our unknowns are the vertical displacement and the torsional rotation of the deck, corresponding respectively to a harmless oscillation and to a very dangerous one. Chapter 3 is devoted to some common features of the three models and the strategy to handle them.
The system of differential equations is studied at first in terms of existence and uniqueness of a solution and subsequently performing numerical analysis on the approximated solution; as we will see the existence and uniqueness topic is not trivial at all due to the nonlinearities, hence we provide the full proofs in the most interesting cases.

Since the dynamics of a bridge is affected by many factors, like the oscillation of the deck, the slackening of the hangers, the displacements of the main cables..., we perform some simplifications. The modeling approach presented in this thesis has to be intended as a process that begins from simple situations and, step by step, goes towards more refined.
At first we suggest a new nonlinear model in which the cables are fixed and the hangers are extensible to focus on the slackening mechanisms of the hangers; in particular, we model this phenomenon through nonlinearities as the positive part function and some variants. We find numerically the solution of the dynamical system, highlighting the instability phenomena with respect to the modes excited and the mechanical parameters.
Then, inspired by the Melan equation we propose a second model for suspension bridges with two deformable cables linked to a deck, through inextensible hangers; in this case we overturn the simplification related to the first model. We prove existence and uniqueness of a weak solution and we perform some numerical experiments on the approximated solution; moreover, we report a sensitivity analysis of the system by mechanical parameters in terms of torsional instability.
Aiming to propose more refined models we conclude this work presenting a third model for suspension bridges in which both the cables and the hangers are deformable, imposing the convexification of the cables. More precisely, we show that, by inserting a convexity constraint on the cables of a suspension bridge, the torsional instability of the deck appears at lower energy thresholds. Since this constraint is suggested by the behavior of real cables, this model appears more reliable than the classical ones. Moreover, it has the advantage to reduce to two the number of degrees of freedom, avoiding to introduce the slackening mechanism of the hangers as an independent variable. The drawback is that the resulting energy functional is extremely complicated, involving the convexification of unknown functions. For these reasons, the chapter devoted to this model is divided in two main parts. The first part focuses on the study of these functionals and provides some new results from calculus of the variations. The second part applies this study to the suspension bridge model with convexified cables, giving the proofs related to existence and uniqueness of a solution and performing different numerical experiments.
Our results display that there are specific thresholds of torsional instability with respect to the initial amplitude of the longitudinal mode excited, suggesting that the origin of the instability is hidden in the nonlinear behavior of structures.

TOPOLOGY OPTIMIZATION: ADVANCED TECHNIQUES FOR NEW CHALLENGES

Nicola Ferro

Supervisor: Prof. Simona Perotto, Prof. Stefano Micheletti

Structural optimization is a research field of large interest and great impact in the community that relies on mathematical methods for the optimal design of structures. Following a standard classification, we distinguish structural optimization in size, shape, and topology optimization. Such techniques have been gaining momentum due to their massive employment for the design by means of new, sophisticated tools, as 3D printing and additive manufacturing (AM). Several fields of application are involved by these new production processes. For instance, automotive and aerospace companies are investing in 3D printing and AM for different design purposes (e.g., design of lightweight and performant components). Other areas of application include architecture, design, fashion and jewelry, which are exploring 3D printing and AM to customize and manufacture original and unique pieces. Moreover, 3D printing is currently one of the cheapest techniques employed for rapid prototyping. In fact, due to the velocity characterizing the process and the contained cost of certain materials (e.g., plastics), it is possible to test several different designs and quickly verify how they perform when manufactured.

In practice, unlike subtractive methods, additive manufacturing consists in the assembly of structures by the deposition (or the melting) of material layer by layer. Additive techniques impact also on the design phase, since they allow to manufacture **free-form structures**, characterized by weaker geometric constraints with respect to the ones typical of subtractive procedures. Virtually all the shapes, even the most complex, can be manufactured, blazing the trail for a novel, free-form design paradigm. Nevertheless, 3D printing and AM are not immune from some issues, e.g., the choice of the optimal orientation for the printing process, the use of supports in the production phase, the presence of inhomogeneities in the printed material derived by the incomplete melting of the powder (as in a laser-based process), just to name a few. These issues are beyond the goals of the thesis and we focus on the reduction of the computational effort demanded in the design phase as well as on the enhancement of mechanical properties and geometric features. In particular, we will address the optimal design problem by means of shape optimization and topology optimization. Shape optimization allows to modify the shape of a given structure to meet prescribed constraints, and to minimize/maximize an objective function related to a mechanical performance, such as the structure compliance or the maximum frequency of vibration. On the contrary, topology optimization seeks the optimal distribution of material inside an initial design domain by changing the topology, without moving the outer structure boundary.

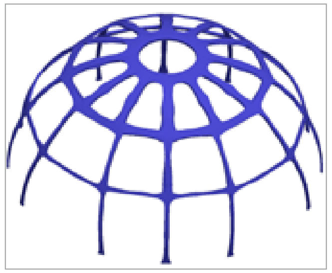

Fig. 1 - Topology optimized structure obtained via SIMPATY algorithm

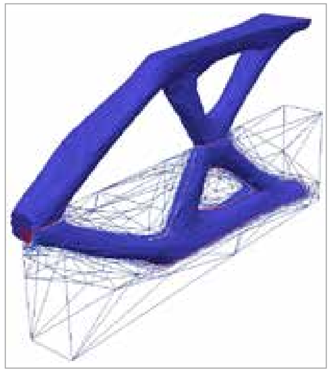

Fig. 2 - Optimized structure and adapted mesh on the simulated quarter of domain

Initially, the mathematical background used throughout the thesis is presented and discussed. In particular, we introduce the standard topology optimization techniques and the advanced mathematical methods used to enhance the classical formulation. We use such tools to deal with the **coupling of a shape optimization procedure with an adaptive algorithm for topology optimization** (SIMPATY) enriched with anisotropic mesh adaptation. The mechanical performance, represented by the static compliance, has been improved by proposing a sequential combination between shape and topology optimization. The results highlight that the structure predicted by the coupled shape-topology optimization algorithm is lighter compared with the result of the shape optimization only, as well as stiffer than the layout provided by the single topology optimization. The additional benefit due to anisotropic mesh adaptation is the creation of very smooth structures characterized by sharp solid/void interfaces. This makes the new designs almost ready to be 3D-printed.

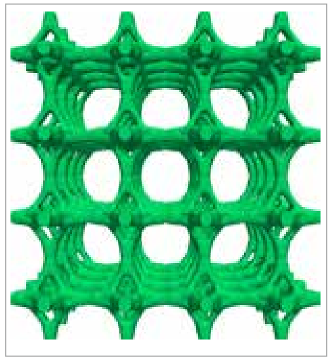

Fig. 3 - A 4-by- 4 pattern of optimized microcellssection plane.

We also propose the application of SIMPATY algorithm to the design of **metamaterials**. The mathematical framework is the **inverse homogenization** theory and the objective is to devise new micro-cells ensuring desired mechanical properties at the macro-scale. The proposed method delivers innovative cell designs as well as standard micro-cells as present in the literature. In all cases, the micro-cells have sharp contours and exhibit the desired effective macroscale properties.
Concerning the reduction of the computational burden involved in topology optimization, we adopted a **POD approach**, properly intertwined with SIMPATY algorithm. The main idea is to use the POD prediction as the initial guess for SIMP enriched with anisotropic mesh adaptation, in the spirit of a predictor/corrector method. This idea considerably reduced the number of iterations for SIMPATY to converge also ensuring similar mechanical performances.
As possible future developments for this work, we list the application of the advanced techniques proposed in this thesis to real-life problems, such as the design of satellite components or prosthetic devices, and the design of new metamaterials enjoying both mechanical and thermal properties. For instance, we aim at enhancing catalytic capabilities for strongly exothermic chemical processes.
From a modeling viewpoint, an extension of the presented algorithms to a more general framework characterized by uncertainty is mandatory with a view to complex applications. We also plan to enrich the formulation of the topology optimization problem with design constraints, to include the manufacturing phase. For instance, in a 3D printing-based design, it is highly desirable to identify the best orientation of the printing plate or the optimal location of the overhangs.

PARAMETRIC AND NONPARAMETRIC FRAILTY SURVIVAL MODELS FOR EXPLORING UNOBSERVED HETEROGENEITY AND PROFILING HEART FAILURE PATIENTS THROUGH ADMINISTRATIVE DATABASES

Francesca Gasperoni - Supervisor: Prof. Anna Maria Paganoni

Clinical administrative databases play an increasingly essential role in medical research to get realworld evidence. Their exploration is particularly relevant for a better investigation of chronic diseases, such as Heart Failure, for which the standard Clinical Randomised Trials are not suitable.

In order to deal with big data, such as clinical administrative databases, novel flexible statistical models and methods are required. In particular, since classical parametric assumptions difficultly hold, nonparametric statistical models should be investigated.

In this PhD thesis, we focused on proposing novel nonparametric approaches in the field of multivariate survival analysis (i.e., multiple and/or hierarchical time-to-event data).

First of all, we focused on hierarchical time-to-event data (i.e., time-to-event data related to grouped statistical units).

In particular, we proposed a nonparametric shared frailty Cox model. The inclusion of a nonparametric discrete frailty term shared among members (i.e., providers) of the same cluster (i.e., latent population) has a two-fold impact: on one hand, we provided a more flexible statistical model to deal with hierarchical time-to-event data, for which parametric assumptions on frailty distribution are usually done (i.e., Gamma of Log-Normal); on the other hand, we provided an in-built clustering technique that is able to detect a second layer of clustering structure that is unknown (i.e., latent populations of providers). Considering its flexibility, this tool is particularly suitable for analysing clinical administrative data in which both unexplained heterogeneity at group level and existence of clusters of groups are suspected. The application to Lombardia Region database revealed the actual potential of this innovative model, indeed we were able to detect the presence of two latent populations of providers and to define their impact on the readmission process (see Fig.1). From a clinical perspective, healthcare providers managers can take advantage of this result to identify providers estimated to be in different latent populations in order to get a better understanding of their features. It worths noting that all the produced software is freely available as a R package.

Moreover, we provided an extension to this model in order to take into account time-dependent covariates that are known at the baseline. In particular, we exploit Functional Data Analysis to deal with regularly measured time-dependent covariates.

Secondly, we focused on a different clinical issue in which multiple outcomes are of interest. Specifically, we explored the whole healthcare path of patients suffering from Heart Failure in Friuli Venezia Giulia region through Semi-Markov multi-state models with transition-specific covariates.

In order to apply these models, a significant preprocessing work was executed. In particular, there was a significant problem of overlapping times between outpatient care and hospitalisations.

Despite of that, we managed to create a suitable dataset and to gain useful conclusions for clinicians. Indeed, we identified different risk factors for readmission in and discharge from hospitals and for survival.

In particular, the ageing process, a multi-morbidity condition and being labelled as a worsening heart failure patient are risk factors (higher risk of readmission and death and a longer in hospital stay). It is interesting that gender is not significant at all, while being hospitalised in a Cardiological Ward is a protective factor with respect to discharge and death.

Similar conclusions can be drawn from the multi-state model that includes also outpatient care structures. In particular, being elder and having multiple comorbidities lead to a shorter length of stay in Integrated Home Care. This is coherent with the fact that more frail patients interrupt outpatient care activations, for being treated in hospitals, that are more suitable structures for more severe conditions. It is also important to notice that gender is significant: males have a higher risk of in hospital readmission but have a lower risk of Intermediate Care Unit activation with respect to females. We can interpret this result by taking into account that females have longer life expectations with respect to males, so widowing state is common. Than, they are the main users of outpatient care, while males are generally treated by their wives, that are the care givers of the family. These results are useful for clinicians, because they got a better insight of the use and the impact of outpatient care on healthcare process of Heart Failure patients.

The third goal of this thesis consists in dealing with an even more complex clinical situation, in which multiple outcomes are of interest and a hierarchical structure of data is recorded. Indeed, we proposed a Semi-Markov multi-state model in which each transition is modelled according to a Cox regression with a nonparametric discrete frailty term. This extension to Semi-Markov models allows us to detect, whether present, a clustering structure in each transition, that are readmission in, discharge from hospital and death. Consequently, we were able to track the path of each provider across transitions and we identified the most frequent patterns of latent populations, that are specific combinations of estimated latent populations. This tool can be exploited by healthcare managers in order to have a deeper insight of providers characteristics across latent populations and also across transitions.

To conclude, we tackled the multi-therapy adherence issue in Heart Failure pharmacoepidemiology. Multiple drugs prescription is a direct consequence of the multi-morbidity condition that characterises Heart Failure patients and it is of great interest to investigate the effect of multitherapy on patients survival. The novel contribution is two-fold: on one hand, we proposed a novel multi-therapy adherence index that is based on administrative database of drug purchase; on the other hand, we investigated patients multi-therapy adherence and we compared the adherence to each drug to European Society of Cardiology guidelines. The results are relevant in clinical framework, since multi-therapy adherence is a protective factor with respect to patients death and the European guidelines are not respected for any drug (at median level). The fact that the proposed multi-therapy index is based on administrative databases has to be highlighted, because it can be reproduced in all regions that collect just the drug purchases, in other words, drug prescriptions information is not needed in this case. The obtained results regarding the comparison with the European guidelines stimulate further exploration on multi-morbidity condition and maybe a revision of the guidelines according to patients complexity can be suggested: this would be a step forward to personalised medicine.

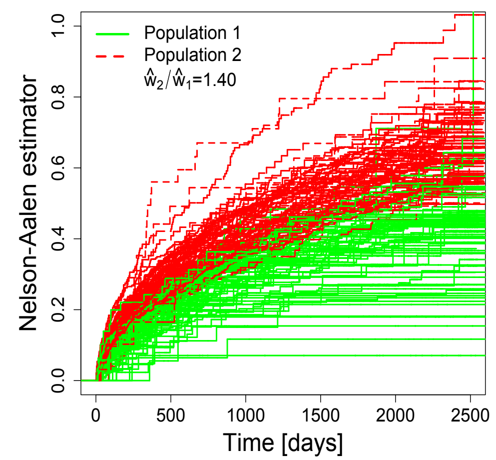

Fig. 1

SEMI-PARAMETRIC MIXED-EFFECTS MODELS FOR ASSESSING PUBLIC EDUCATION SYSTEMS

Chiara Masci – Supervisor: Prof. Anna Maria Paganoni

This PhD research regards the development of innovative statistical models and methods and their application to administrative educational databases for the analysis of students, classes, schools and universities performances. The research aims go in two directions: the former is to individuate existing statistical methods that have the potential of being applied to educational data to address new and interesting research questions; the latter is to develop statistical models and methods that represent a novelty and a value-added both in the technical and in the educational literature panorama. The educational databases object of our studies regards both lower and higher education. The two administrative lower educational databases are the Italian Institute for the Educational Evaluation of Instruction and Training (INVALSI) database and the Programme for International Student Assessment (OECD-PISA) database. The higher educational database regards the careers of students enrolled in the Bachelor of Science of Politecnico di Milano. The main characteristic of the data collected in these databases is their hierarchical structure (e.g. students are nested within classes/courses, that are in turn nested within schools/universities) and our aim, cross-sectional to all our proposed works, is to analyse these data by means of statistical models able to take into account their nested nature. This is the reason why our modelling approach is based on mixed-effects (or multilevel) models, able to disentangle the effects given to each level of grouping of data. Parametric mixed-effects models have been broadly applied in the educational context, but our innovative approach consists in relaxing some of the model parametric assumptions, both on fixed and random effects. The aim is to develop innovative statistical methods able to address new and complex research questions and to deal with some of the restrictions and weak points of the existing parametric models. In particular, Figure 1 represents our contribution in the mixed-effects models panorama.

We propose four different research lines. The first research line regards the application of random-effects regression trees and boosted regression trees to the OECD-PISA database. In a methodological perspective, we apply a method that relaxes the parametric assumption on the fixed effects of linear mixed-effects models, replacing the linear functional form of the fixed effects by a regression tree. The flexibility of the model obtained by doing this results to be of great advantage in easily modelling both non-linearities and interactions among the variables. When applied to worldwide educational data, this methodology allows the identification of complex patterns across the variables and gives an improved description of the structurally different educational production functions across countries, leading to new and interesting insights in a policy implications perspective. Applying mixed-effects regression trees to OECD-PISA data, we individuate student level characteristics associated to student performances and we estimate school value-added, that, in a second step, can be characterized in terms of school level variables by means of boosted regression trees. Besides the important findings of the study, a further advantage of the approach regards the easy interpretability and communicability of these findings.

The second research line regards the modelling of university student dropout, by means of a novel statistical method, that is a generalization of mixed-effects trees for a response variable in the exponential family: Generalized Mixed-Effects Trees (GMET). We show in a simulation study the performance of our proposed method, comparing GMET to classical models and highlighting its advantages. We apply GMET to model Bachelor student dropout in different degree programmes of Politecnico di Milano. Results show that the model is able to identify discriminating student characteristics and estimate the degree programme effect on the probability of student dropout.

The third research line regards the development of a semi-parametric mixed-effects linear model, together with an EM algorithm to estimate its parameters, and its application to the INVALSI database as a tool to perform an unsupervised classification of Italian schools. We relax the parametric assumption on the distribution of the random effects of mixed-effects models and we assume them to follow a discrete distribution with an a priori unknown number of support points. This modelling induces an automatic clustering of the higher level of hierarchy (enabling the identification of subpopulations) and can be used in multiple classification problems. Among being an innovative method in the statistical scenario and representing a significant value-added in the context of mixed-effects models, this model improves the research on school effectiveness since, when applied to INVASI data considering students nested within schools, it identifies subpopulations of schools that differ in terms of distribution of student outcomes and that can be characterized a posteriori by school level variables.

The last research line evolves as an extension of the second one, since it regards the development of the bivariate version of the semi-parametric mixed-effects linear model (i.e. with a bivariate response variable) discussed in the previous point. In our proposed bivariate semi-parametric mixed-effects models, the random effects are assumed to follow a bivariate discrete distribution where the numbers of support points are unknown and allowed to be different between the two responses. This modelling enables to jointly model the presence of bivariate subpopulations in the higher level of hierarchy and it is totally new to the literature both from a technical/statistical point of view and for the potential that modelling the joint distributions of the identified subpopulations has from an interpretative point of view. When applied to INVALSI data considering students nested within classes, this model allows to identify subpopulations of classes that differ in their joint effect on reading and mathematics student achievements.

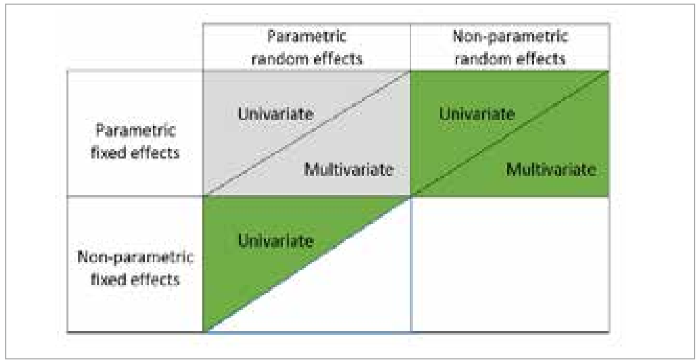

Fig. 1 - Scenario of mixed-effects models in education. Grey box represents existing statistical models already applied in the educational field while green boxes represent our novel contribution to the literature, both in the methodology and in the application.

ON THE DETERMINATION OF DISCONTINUOUS COEFFICIENTS IN SEMILINEAR ELLIPTIC AND PARABOLIC BOUNDARY VALUE PROBLEMS ARISING IN CARDIAC ELECTROPHYSIOLOGY

Luca Ratti - Advisor: Prof. Elena Beretta

Co-Advisor: Prof. Marco Verani

The objective of my thesis is the investigation of inverse problems related to semilinear boundary value problems involved with the mathematical description of the cardiac electrical activity. The long-term purpose which motivates the research in this field is to discuss the possibility of identifying ischemic areas within the cardiac tissue only by means of non-invasive measurements. We tackle this issue within the mathematical framework of the theory of Inverse Problems, pursuing an approach which focuses both on analytical and on numerical aspects.

Mathematical models allowing for a satisfactory description of the cardiac electrophysiology have been developed since the late 70s, based on homogenization arguments. In particular, the *monodomain* model, allowing for a detailed description of the evolution of the transmembrane electrical potential in the myocardial tissue, consists in a coupled system of a semilinear parabolic partial differential equation and an ordinary differential equation. When considering the presence of ischemic areas within the tissue, discontinuous alterations of the coefficients are entailed: we consider the inverse problem of determining such inhomogeneities from the knowledge of the electrical potential on the boundary of the domain.

Despite some contributions have been recently given in this field, a complete theoretical investigation of this inverse problem has not yet been carried out. In particular, due to the shortage of measurements at disposal, this can be considered an ill-posed inverse problem: indeed, our purpose is to reconstruct ischemic areas from a single measurement of the boundary voltage induced by the electrical activity during the heartbeat. Moreover, despite the connections with widely studied inverse problems related to the detection of unknown coefficients (as the Calderon or inverse conductivity problem), the nonlinearity of the direct problem implies significant restrictions to the application of existing techniques. As a consequence, it is necessary to extend and design novel methods for the problem of interest, both for analytical and reconstruction purposes.

The main guidelines of this study are both the extension of the existing theoretical results and the development of effective and rigorous numerical reconstruction algorithms. We proceed by formulating simplified versions of the problem of interest and then extending the results on subsequent refinements of the model. We also rely on the introduction of regularization hypotheses, namely, a priori assumptions regarding the inhomogeneity to be identified, which help in restoring the well-posedness of the inverse problem: particular attention is given to the task of localizing ischemic areas of small size.

Localization of small inclusions in semilinear boundary value problems. Under the regularization hypothesis that the inclusion to be identified is small with respect to the size of the domain, we have been able to prove rigorous results regarding the analysis of the inverse problem. Specifically, both in a simplified elliptic and parabolic case, we have derived an asymptotic expansion of the boundary electrical potential with respect to the size of the inclusion, also entailing a local stability estimate for the inverse problem in the elliptic case. We have employed such results also to devise a numerical algorithm for the localization of the ischemia, based on the topological optimization of a suitable cost functional.

Detection of large inclusions in semilinear boundary value problems. When removing any *a priori* assumption and tackling the detection of arbitrarily large inclusions, no theoretical result regarding the well-posedness of the inverse problem is known. We instead focus on the rigorous deduction of a reconstruction algorithm for the approximation of its solution. The devised technique, which relies both on the regularization theory for inverse problems and on a relaxation strategy, allows for satisfactory reconstructions. We have investigated the convergence of the proposed algorithm, and we have reported a detailed comparison with some state-of-the-art alternative approaches. Moreover, due to its generality and feasibility, this technique is likely to be extended to a wider class of identification problems.

Preliminary results for the analysis of the inverse monodomain problem. The final purpose of the thesis is to pave the way for the application of the introduced analytical and numerical techniques on the full complexity of the application model. We first investigate the well-posedness of the direct problem, focusing on comparison and regularity properties and extending the existing results in literature. An additional aspect which is taken into account, from a numerical perspective, is the *a posteriori* error analysis of the discrete solver of the direct problem, which is performed by introducing suitable computable estimators. This study is preliminary for the formulation of adaptive algorithms for the numerical solution of the direct problem, and ultimately for the efficient application of the developed reconstruction algorithms.

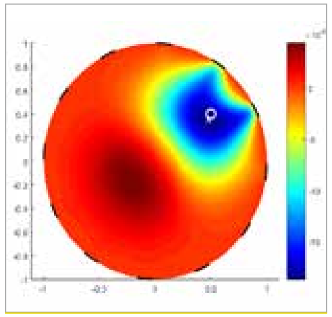

Fig. 1 - Detection of a small inclusion from partial measurements - elliptic case

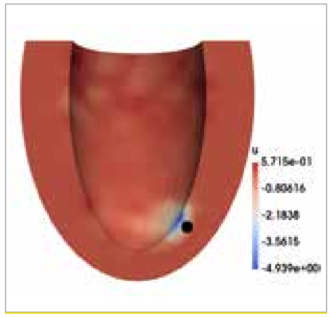

Fig. 2 - Detection of a small inclusion from noisy measurements - parabolic case

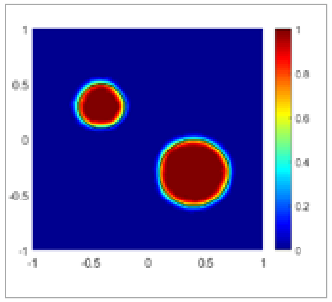

Fig. 3 - Detection of a large inclusion

MATHEMATICAL MODELLING OF SOFT AND ACTIVE MATTER

Davide Riccobelli - Advisor: Prof. Pasquale Ciarletta

This thesis focuses on the mathematical modelling of soft and active solid matter using continuum mechanics. An elastic body is said to be soft if it can undergo large deformations; it is said to posses an active behaviour when it can rearrange its micro-structure in presence of external stimuli, not necessarily of mechanical nature. Examples of active processes are biological growth or the contraction of dielectric elastomers provoked by an electromagnetic field.
The research activities undertaken concerned both analytical and numerical tasks to solve some physical problems in this field.
In particular, we focused on:

- the constitutive theory of soft materials with initial stresses,
- the mathematical modelling of active phenomena in biological matter,
- the formation of patterns in soft solids due to a mechanical instability.

The thesis is organized as follows. In Chapter 1, we briefly expose some basic notions of non-linear elasticity. We review the fundamental literature on the mathematical modelling of biological growth and muscle contraction, and on an emerging field in mechanics, called morpho-elasticity.
In Chapter 2, we investigate the mathematical description of elastic bodies possessing a non-vanishing distribution of initial stress, i.e. the Cauchy stress in the undeformed reference configuration. We provide new mathematical and physical interpretations of the required constitutive restrictions, proving the existence of energy minimizers in the framework of the theory of initially stressed materials.
In Chapter 3, we propose new mathematical models of active processes in soft biological matter, particularly focusing on tumour growth and muscular contraction. We show that it is not possible to recover the experimental stress-stretch curve corresponding to a uniaxial deformation of a skeletal muscle using the active strain method, based on a multiplicative decomposition of the deformation gradient. Instead, we propose an alternative model based on a mixture approach, called *mixture active strain*. Moreover, we show that solid tumours behave as growing poroelastic materials, where the growth is modulated by a chemo-mechanical feedback. The results of our model are in very good agreement with both *in-vitro* and *ex-vivo* experimental data.
In Chapter 4, we model morpho-elastic phenomena in both living and inert soft matter. First, we investigate the mechanics of tumour capillaries, showing that the incompatible axial growth of the straight vessel can trigger an elastic instability, generating a tortuous shape.
Second, we study how residual stresses can induce mechanical instabilities in soft spheres, e.g. in growing tumour masses. Considering several spatial distributions of the residual stress field, we prove that different topological transitions occur in the sphere where the hoop residual stress reaches its maximum compressive value.
Third, we show that gravity bulk force can cause an elastic instability in soft elastic bilayers. We show that the non-linear elastic effects saturate the dynamic instability of the bifurcated solutions that characterize fluid-like matter, displaying a rich morphological diagram where both digitations and stable wrinkling can emerge.
Finally, the results of this thesis prove how the combination of nonlinearities and nonconvexity in elastic mixed boundary value problems may emerge as complex physical phenomena, whose understanding requires the development of novel mathematical tools (Chapter 5).

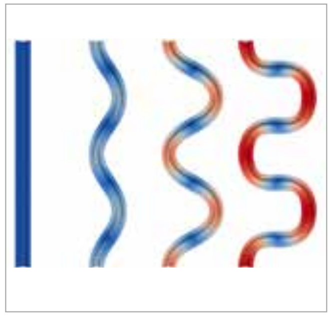

Fig. 1 - Evolution of the morphology of a growing tumour capillary.

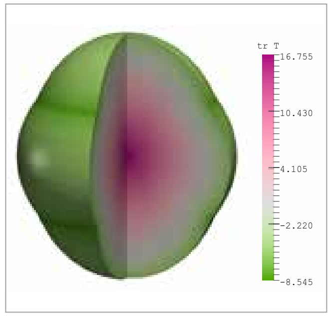

Fig. 2 - Buckled configuration of a sphere sujected to residual stress.