Abstract dei progetti FIS 3

Application of Artificial Intelligence in Diagnostics of Thyroid Nodules
PI: Prete Alessandro
Starting Grant
LS4

The incidence of thyroid nodules has been increasing, reaching up to 30%, mainly due to incidental diagnoses. Despite the low clinical impact of most nodules, over 160,000 fine-needle aspiration cytologies (FNAC) are performed annually in Italy, leading to interpretation challenges and high healthcare costs. Less than 5% of thyroid nodules are malignant, yet the rising diagnosis of thyroid cancer is projected to increase the overall societal cost in the U.S. to $3.5 billion. International guidelines aim to reduce overdiagnosis. Ultrasound-based risk stratification systems guide diagnostic and therapeutic decisions, though their realworld application remains suboptimal. Molecular analyses offer high negative predictive value but require additional FNAC sampling and entail significant costs, creating social disparities. Artificial intelligence (AI) is emerging as a valuable tool for integrating clinical, biochemical, and molecular data. Some AI algorithms have been developed for thyroid diseases, showing potential in improving diagnostic accuracy. However, existing studies have limitations, including retrospective designs, lack of validation cohorts, and small sample sizes, making AI applications in thyroid disease still challenging.

This project proposes a 5-years, prospective, observational, single-center study. It will be conducted at the Department of Clinical and Experimental Medicine of University of Pisa in collaboration with the Department of Information Engineering. The project will be structured in 2 milestones. Milestone 1 aims to develop and validate the "Cyto" AI algorithm to predict thyroid nodules cytology upon ultrasound (US) images. It involves recruiting 15,000 patients, subgrouped in training (6000 patients) and validation (9000 patients) cohorts. Milestone 2 focuses on a cluster of 1,500 patients with indeterminate or malignant thyroid nodules, subgrouped in training (600 patients) and validation (900 patients) cohorts; it aims to develop and validate the “Molecular” AI algorithm to predict somatic mutations of thyroid nodules, integrating US and cytological images. By leveraging AI, this study aims to address the clinical and social burden of thyroid nodules, enhancing diagnostic precision, reducing unnecessary procedures, and improving patient outcomes.

DYNamic scAling in vitro: a novel stochastic paradigM for characterizing cellular processes across dImensionaliTiEs
PI: Botte Ermes
Starting Grant
LS9

Allometric scaling has been largely recognized as a universal property of biological populations. Current scaling laws – such as the well-established Kleiber’s law – relate specific phenotypic traits to size, describing self-similarities across dimensionally different systems. However, longstanding evidence also suggests the influence of the observation time on biological processes, which may underly timescale invariance over individual growth.

In this context, DYNAMITE integrates bioengineering with experimental biology, statistical methods and computational modelling to assess whether cellular systems *in vitro* exhibit dynamic scaling, *i.e.*, self-similarity of biophysical features across timescales. My hypothesis is indeed that time-dependent scaling behaviours can emerge in cell cultures, providing a novel paradigm to describe fundamental characteristics of human cells *in vitro*.

Recognizing that variability is ubiquitous in biological populations, I will establish a dynamic scaling framework which incorporates intrinsic phenotypic fluctuations. The framework will be first

formulated for hepatic cells cultured in monolayers and validated by measuring covariations of their structural, functional and behavioural traits with the observation time. For this purpose, I will rely on cutting-edge sensing and imaging approaches, integrated with advanced *in silico* modelling and data processing to identify scaling parameters according to the proposed stochastic formulation. Once verified, I will target the extension of the DYNAMITE framework to liver *in vitro* models across dimensionalities (*i.e.*, single cells and liver organoids), explicitly accounting for the potential impact of the spatial arrangement of cells on their time-dependent scaling and hence delivering a unifying formulation with broader applicability.
As a proof of concept, DYNAMITE will apply its general framework to evaluate the efficacy of chemotherapy treatments for liver cancer. Embracing recent theories which surmise that cells perceive time as a function of their surroundings, the project will benchmark how cancer cells and tumoroids change their dynamic scaling in response to microenvironmental alterations associated with different doses of chemotherapeutic agents. A significant shift of scaling parameters might represent a useful quantitative metrics to improve drug assessment.
Unveiling emergent scaling of cellular dynamics with time and elucidating its link with biological fluctuations and cell packing, DYNAMITE will define a scaling paradigm complementary to traditional size-related allometries. Their combination will offer an intriguing toolkit for investigating common functional or behavioural patterns across both size- and timescales, enhancing the translatability of *in vitro* findings to the clinical context and reducing reliance on animal experiments.

Investigation on Feline Betaretrovirus Infection, Pathogenesis and Missing Piece Hypothesis
PI: Parisi Francesca
Starting Grant
LS9
Over the past decades, the identification of a human betaretrovirus (HBRV) has strengthened the hypothesis that viral agents may be involved in some human diseases, including breast cancer and primary biliary cholangitis. This virus shares similarities with Mouse Mammary Tumour Virus (MMTV), a well-established oncogenic virus involved in mammary tumors in mice. Studies in cats have detected MMTV-like viral sequences and protein expression in feline mammary carcinomas and lymphomas, suggesting the possible involvement of a betaretrovirus in some feline diseases.

Within this context, FELINE BETA aims to investigate the possible role of a betaretrovirus in feline mammary tumors and inflammatory liver diseases through a research framework that combines the detection and characterization of viral sequences, the assessment of viral biological activity, the study of virus-host interactions, and the analysis of the associated pathogenetic mechanisms. The project will investigate mammary tumors, inflammatory liver lesions, and different biological specimens collected non-invasively or as part of routine clinical practice. Through an integrated approach combining histopathology, immunohistochemistry, immunoenzymatic assays, molecular analyses, and genomic and transcriptomic investigations, FELINE BETA will integrate pathological, immunological, and molecular data to investigate possible pathogenetic mechanisms associated with the virus in some feline diseases. The project also includes the optimization of innovative, standardized, and shareable methodologies for the detection of viral sequences.
FELINE BETA may contribute to advancing knowledge in feline pathology and support new strategies for prevention and clinical management. The project will also strengthen the role of the cat as a spontaneous model for investigating mechanisms of viral pathogenesis and comparative medicine, opening new perspectives for animal health and One Health-oriented research.

Rational points by fundamental groups
PI: Bresciani Giulio
Starting Grant
PE1
In 1983, G. Faltings proved the Mordell conjecture: hyperbolic algebraic curves have a finite number of rational points. In the same year, A. Grothendieck wrote
him a letter, in which he conjectured a deep link between the rational points of hyperbolic algebraic curves over global fields to their étale fundamental groups.
Nowadays, this is called the Section Conjecture.
Recent breakthroughs are beginning to shed some light on this problem. In 2005, Koenigsmann proved a birational analogue over p-adic fields. In 2008, J. Stix
produced the first meaningful examples of curves satisfying the conjecture. My work in 2022 demonstrated a birational version of the Section Conjecture over
global fields.
In 2024, I introduced an enriched version of the étale fundamental group - namely, the toric fundamental group - as a new tool to attack the Section Conjecture.
There is a version of the Section Conjecture for the toric fundamental group, the Toric Section Conjecture. The Toric Section Conjecture is much more within
reach than the original conjecture; in particular, I am extremely close to proving the Toric Section Conjecture over p-adic fields. At the same time, the Toric
Section Conjecture is so close to the original one that its resolution will lead to major breakthroughs in the study of the Section Conjecture.
The first part of the project is designed to reach three goals, each being the starting point for the next one.
1. Prove the Toric Section Conjecture over p-adic fields.
2. Prove the Toric Section Conjecture over global fields.
3. Over global fields, pass from the toric setting to the original étale framework.
Reaching any of the three goals would be a breakthrough. Reaching all of them would mean having a proof of the Section Conjecture.
In the second part of the project, I propose to develop the newly emerging field of the Arithmetic of Gerbes, which will consolidate our understanding of the
Section Conjecture.

Topology and geometry of higher Teichmuller spaces
PI: Tamburelli Andrea
Starting Grant
PE1
Higher Teichmüller theory studies special spaces of surface group representations into higher-rank Lie groups and lies at the intersection of differential geometry, topology, geometric analysis, and dynamical systems. While these spaces generalize many features of classical Teichmüller theory, several fundamental questions remain open, particularly concerning their compactification, global geometry, and interactions through geometric transitions. The TARGETS project aims to develop a unified framework to address these problems through methods combining Higgs bundles, harmonic maps, minimal surface theory, and geometric limits.

The first objective is to construct geometrically meaningful compactifications of higher Teichmüller spaces, especially Hitchin components, and provide explicit descriptions of their boundary points.

The project proposes a novel approach based on equivariant harmonic maps and their limits in Euclidean buildings, with the goal of identifying boundary objects as mixed geometric structures combining generalized translation surfaces and vector-valued laminations. This would extend classical compactification results from Teichmüller theory to higher rank settings.

The second objective is to investigate the global geometry of higher Teichmüller spaces through the introduction and analysis of mapping class group invariant pseudo-Kähler structures compatible with Goldman's symplectic form. The project will study their curvature, completeness properties, and geometric significance, with particular focus on rank-two cases such as Hitchin components for SL(3,R) and related representation spaces.

The third objective is to develop new examples of geometric transitions between character varieties and determine how geometric structures evolve across such transitions. In particular, the project seeks to establish transitions linking different higher Teichmüller spaces while preserving or deforming their associated pseudo-Kähler geometries.

The expected outcomes will provide new insight into the geometry and topology of higher Teichmüller spaces, the action of mapping class groups, and the geometric meaning of Higgs bundle parametrizations, opening new directions for the study of moduli spaces and geometric structures.

New Materials and Methods for the Fabrication of Organic Electronic Components on Complex Substrates

PI: Carlotti Marco

Starting Grant

PE5

While electronic components based on organic semiconductors cannot compete directly with the performances and lifetime of their silicon counterparts, they offer appealing opportunities in terms of compliance with non-rigid substrates and fabrication technologies, enabling cost-effective and high-throughput solution based processes. However, these latter mostly rely on 2(.5)D lithographic and printing techniques, limiting their circuital design to flat substrates. The possibility of employing freely the third dimension would offer a disruptive divergence between organic and silicon-based devices.

In this context, the MATRIX project aims to revolutionize the design of functional microdevices by developing innovative materials and microfabrication

methodologies that can allow the direct integration of organic electronic components on substrates and architectures with non-flat geometries via highresolution 3D microlithographic approaches.

Volumetric lithographic printing of organic semiconductors—in most cases comprising materials with a high degree of conjugation—is not straightforward because of their high extinction coefficients and broad absorption profiles, which limit light penetration and can cause unwanted heating and degradation.

To overcome these issues, during the MATRIX project, I will design innovative polymeric precursors characterized by non-conjugated backbones and suitable absorption profiles, from which one can generate and immobilize the desired semiconductors through selective photoreactions promoted by Direct Laser Writing (DLW).

The latter is a powerful mask-less 3D microlithographic technique capable of combining sub-100 nm resolution, true 3D freedom, and high throughput that employs nonlinear absorption phenomena to trigger light-promoted processes in small regions of space. In combination with the development of novel methodologies for the reliable fabrication of electrodes and connections on non-horizontal substrates and microstructures, the project aims to set a new paradigm for the direct integration of electronic components and logic gates on soft and hybrid microsystems without limitations posed by their 3D architecture, paving the way for disruptive advances in functional microdevices and soft robotics.

Calcite and allanite Recoverying Uranium: from Structural mapping to Tectonic implications
PI: Di Rosa Maria
Starting Grant
PE10

Extensional faults linked to the opening of the Tyrrhenian back-arc basin are known for their antimony, arsenic and zinc sulfide mineralization. They were exploited in the first half of the last century, and are currently classified by the European Union as critical raw materials. This mineralization derives from mantle and lower crust- derived fluids, whose transfer to shallower crustal levels was driven by the activation of extensional faults. During their ascent along these fault zones, such fluids mixed their composition with others of meteoric origin, determining the precipitation of a carbonate gangue always associated with this mineralization. The carbonates that form this gangue, mainly calcite, dolomite and ankerite, show a positive anomaly in uranium, which make them a powerful tool for U-Pb dating. Another uranium- bearing mineral found along these faults is allanite, which is known for its characteristic resistance to hydrothermal alteration as well as overpressure effects typical of shear zones.

The CRUST project aims to characterize extensional faults hosting sulfides mineralization located in the peri-Tyrrhenian area (Alpine Corsica, Northern Apennines), in order to understand and constrain in time the tectonic processes that formed them. To do this, with CRUST a new methodology based on structural geology, geochemistry and geochronology will be defined, capable of characterizing this type of mineralizations in different geological settings. In particular, the CRUST approach will be tested in other extensional contexts such as the Shkoder-Peja Normal Fault (North Albania), the Kerdylion detachment (North Greece) and the atypical case of Lengenbach (Switzerland), in which the Triassic sulfide mineralization predated the Alpine orogeny. Finally, the methodology will be applied to two Carlin-type deposits (Nevada, China), whose geochemical and structural features only partially overlap with that of the CRUST case studies.

Unveiling Latin through non-literary texts: continuity and discontinuity in language change
PI: Tamponi Lucia
Starting Grant
SH4

The project ULTRA (Unveiling Latin through Non-Literary Texts) investigates linguistic variation and change in the history of Latin through the analysis of non-literary texts from Italy, spanning from the 7th century BC to the 13th century AD. By focusing on documentary sources such as inscriptions, papyri, graffiti, and charters, the project aims to reconstruct processes of linguistic continuity and discontinuity that are often obscured in literary texts.
ULTRA will create a large-scale open-access database integrating and annotating all digitized dated non-literary Latin texts from Italy – over 130,000 texts and approximately 6 million words. The project will consolidate existing digital resources, harmonize metadata and implement lemmatization and

part-of-speech tagging using advanced NLP and AI-based methods, enabling complex and previously inaccessible linguistic queries.
The project will provide a multidimensional perspective on linguistic variation in Latin, distinguishing between internally and externally driven change related to diatopic, diastratic, and diaphasic dimensions. This framework will support analyses of grapho-phonological, morphosyntactic, and semantic developments across time, combining approaches from historical linguistics, philology, and computational methods in both quantitative and qualitative investigations.
Expected outcomes include new insights into the mechanisms of language change, the refinement of methodologies for the study of ancient languages, and the development of reusable digital tools applicable to other linguistic traditions. The resulting open-access infrastructure will foster interdisciplinary collaboration and improve accessibility for scholars, educators, and the broader public.

Optimal TranspOrt and large Deviations for Deep LEarning theory
PI: Trevisan Dario
Consolidator Grant
PE1
Artificial intelligence promises a widespread revolution, demonstrating already exceptional capabilities across a multitude of fields, including natural language processing, computer vision, and complex problem-solving. The iterative nature of machine learning techniques has led to unprecedented advancements, allowing statistical models to continuously improve and adapt. On the theoretical side, despite significant progress, however, a comprehensive understanding of models based on deep neural networks remains elusive. This gap in knowledge may obscure critical insights that could further enhance the effectiveness and reliability of these systems.

OTODDLE proposes a novel framework that integrates Large Deviations Theory and Optimal Transport to systematically address such theoretical shortcomings. At its core, it aims to develop Wasserstein-like metrics to enable a quantitative analysis of deep learning models, beyond traditional Gaussian kernel approximations. This will allow understanding rare events that have low probability but can have significant implications for neural networks during training and deployment, across various architectures and learning algorithms.

OTODDLE will establish new connections between the theory of neural networks and the mathematical fields of calculus of variations and partial differential equations. This interdisciplinary approach will encourage collaboration across analysis, probability, and mathematical statistics. On the applied side, by probing how of foundational algorithms, like importance sampling, the project will lead to more advanced numerical schemes and better training methodologies for machine learning, improving the robustness of neural networks. Ultimately, OTODDLE will develop effective theoretical tools for real-world applications in complex systems, opening new avenues for future experts in related fields.

Bootstrapping Quantum Field Theories
PI: Vichi Alessandro
Advanced Grant
PE2
Quantum Field Theory (QFT) provides the universal language for describing fundamental interactions and collective phenomena, yet its strongly coupled regimes often remain inaccessible to conventional perturbative methods. The bootstrap approach offers a radically different strategy: instead of starting from a microscopic Lagrangian, it combines symmetry, quantum unitarity and consistency conditions to determine or constrain the space of possible theories. Recent analytical and numerical advances

have demonstrated the remarkable power of this philosophy, but many central problems—including gauge theories, generic two-dimensional conformal field theories and realistic scattering amplitudes—remain largely unexplored.

QBOOT aims to substantially extend the reach of the bootstrap and develop new non-perturbative tools for QFTs in two, three and four dimensions. The project will pursue five interconnected directions. First, it will investigate infrared fixed points of three- and four-dimensional gauge theories, determining critical observables, mapping their phase diagrams and clarifying how conformality is lost as the matter content is varied. Second, it will use the AdS/CFT correspondence to translate rigorous conformal-bootstrap results into constraints on quantum field theories in Anti-de Sitter space, with particular emphasis on non-perturbative gauge interactions.

QBOOT will also develop an amplitude bootstrap for large-N QCD, where mesons and glueballs become stable and their scattering amplitudes obey powerful analyticity, crossing and positivity constraints. Extensive systems of dispersion relations will be used to bound low-energy couplings and constrain the spectrum and interactions of hadrons, including mixed processes involving massive and spinning states. Finally, the project will explore positivity bounds for effective field theories of gravity and matter, addressing how strongly consistency conditions restrict modifications of gravity and whether weak coupling and unitarity can force the emergence of string-like behaviour.

Throughout these directions, QBOOT will combine new theoretical insights with efficient optimisation algorithms and complementary numerical methods. The project is expected to deliver quantitative information about strongly coupled gauge theories, large-N QCD and gravitational effective theories, while establishing broadly applicable strategies for the non-perturbative study of quantum field theory.

Communicating Justice: Courts, Public Opinion and the Transformation of the Public Sphere
PI: Sperti Angioletta
Advanced Grant
SH2
COMMJUST analyses the institutional communication of ordinary, supreme and international courts, and its impact on democratic legitimacy, public trust in justice, and perceptions of the impartiality of the judiciary.

The project responds to the growing presence of courts in the public sphere and to their increasing use of more direct forms of communication, including institutional websites, press releases and social media. From a comparative perspective, COMMJUST examines national courts in Italy, Germany, France, the United Kingdom and the United States, together with the Court of Justice of the European Union and the European Court of Human Rights.

The research adopts an interdisciplinary approach, combining comparative constitutional law, sociology, media and journalism studies, and political science. A key innovative feature of the project is the use of artificial intelligence to conduct large-scale analysis of courts' communication, with the aim of identifying patterns, strategies and trends that are not easily detectable through traditional methods.

COMMJUST aims to provide new theoretical and empirical tools for understanding how judicial communication affects trust in justice, perceptions of courts' independence, and their role in promoting the rule of law and democratic values.

Medicine as Social Practice: An Archaeology of Health and Diseases in Ancient Egypt
PI: Miniaci Gianluca
Advanced Grant
SH6
The SENEB project aims to provide a new, social dimension in the study of ancient human medicine, taking as case study ancient Egypt in the second millennium BC, for its large amount of sources (textual/artefactual/biological/archaeological). Recent historical events have confirmed that health, both in its ideological and practical aspects, is a fundamental component of any human society and community. The effects of disease affect not only the human body, but also social dynamics, human relationships and the economy, involving the accessibility of treatment, the availability of remedies, the professionalism of the physician and the concept of health and disease. The study of health and healing is therefore fundamental to understanding a society, its problems and inequalities, its ideology and approaches to a fundamental aspect of everyday life. The study of ancient healing practice has been too often isolated from the study of other society components/aspects and used to "promote" a sort of continuous cognitive and social evolution in comparison with our current knowledge. Drawing on the experience of the PI in the study of ancient Egyptian society and his recent research in magico-medical tools (clay figurines used as physician's instruments), SENEB aims to overcome the traditional etic, isolating approach to the study of ancient medicine in order to insert it in its social experience, without the predetermined separation of magic, religion and science. Research will benefit from a variety of innovative approaches: study and re-evaluation of textual sources to reconstruct the role of healer and patient and the cultural, social background of healing know-how; analysis of objects to assess clear parameters for the identification of healing practice in the archaeological record;
study of settlement features to assess the impact of the environment and urban life on personal health; application of the palaeopathological analysis of human remains to the concepts of bioarchaeology of care and bioarchaeology of disability. The data will be analysed according to regional and chronological differences and integrated according to the principle of intersectionality in order to reconstruct individual perceptions of health and illness and the social and cultural visualisation of personal experience

Lives in Motion: Belonging and Otherness. Women, Minors, and Statelessness in the Context of Radicalization
PI: Pepicelli Renata
Advanced Grant
SH8
A decade after the 2015 security crisis that impacted Southwest Asia and North Africa (SWANA) and Europe, women's participation in Salafi-jihadi networks has become a defining aspect of contemporary jihadist movements. Women from both Eastern and Western countries played a pivotal role in sustaining the so-called Islamic State, challenging traditional gendered narratives within both the SWANA region's cultural frameworks and the global discourse on terrorism.
The collapse of the Islamic State in 2019 left many women and minors associated with ISIS stranded in Syrian and Iraqi refugee and IDP camps without citizenship or the right to return. For those repatriated, reintegration presents significant challenges. Experiences of radicalization, political violence, and war continue to shape reintegration processes, while policy frameworks often struggle to address their return.
Prevailing narratives often portray women associated with ISIS as either passive victims or irredeemable threats, failing to capture the complexities of their experiences and agency. Despite growing research on women in jihadist movements and debates on their agency, the intersection of radicalization, belonging, statelessness, otherness, and reintegration remains underexplored, while studies focusing on minors are even more limited. This project fills this gap by adopting a gendered,

intergenerational, and interdisciplinary lens to examine self-representations, interactions with media narratives, and the legal obstacles affecting the reintegration of women and minors into their countries of origin.
Focusing on the cases of Syria, Iraq, Jordan, and Tunisia in the Arab region, and France and the United Kingdom in Europe, the research employs literature review, critical discourse analysis, ethnographic methods, and oral history. Given the global security landscape and the urgent need for policies balancing security and human rights, this research offers critical insights for academia and policymakers.