



PhD in BIOINGEGNERIA / BIOENGINEERING - 40th cycle

PNRR 629 PA Research Field: A MICROMECHANICAL MODEL OF THE HUMAN RETINA TO GUIDE GENIC THERAPY INJECTIONS

Monthly net income of PhDscholarship (max 36 months)
€ 1400.0
In case of a change of the welfare rates during the three-year period, the amount could be modified.

Context of the research activity	
Motivation and objectives of the research in this field	<p>Hereditary retinal diseases (iRDs) are the leading cause of blindness among working-age adults. Retinal gene therapy (RGT) is the only approach capable of treating some forms of iRDs, which motivates significant effort in developing RGT products for other forms of iRDs. Drug administration occurs through subretinal injection, which is a high-risk procedure for retinal damage. The lack of a standardized and safe surgical administration approach limits the use of RGT. Available gene delivery models focus solely on estimating effective doses for subretinal injections. Our hypothesis is that injection-induced damage results from processes damaging various microstructural components of the retina at different scales. We propose developing a micromechanical in silico model of the retina supported by experimental measurements of both macroscopic and local mechanical properties of the tissue. This information will be useful to create a quantitative scenario for drafting guidelines for gene delivery therapies for retinal disorders.</p>
Methods and techniques that will be developed and used to carry out the research	<p>The thesis development involves innovative experimental techniques, including micro-indentation tests and atomic force microscopy (AFM) for macroscopic and microscopic characterization of mechanical properties, respectively. Additionally, a novel experimental setup simulating subretinal injections coupled with confocal laser scanning</p>



	<p>subretinal injections coupled with confocal laser scanning microscopy will capture alterations and ruptures during injections.</p> <p>The experimental results will guide the creation and implementation of the micromechanical model, which will be calibrated using numerical simulations and experimental data from micro-indentation tests. Ultimately, the ability of the model to predict retinal mechanical behavior under subretinal injection conditions will be evaluated through numerical simulations, validated against intraoperative optical coherence tomography (OCT) images provided by clinical collaborators.</p>
<p>Educational objectives</p>	<p>The PhD candidate will learn</p> <ol style="list-style-type: none"> 1) to perform micromechanical indentation and multiaxial tests on retinal tissue; 2) to use AFM and confocal microscopy; 3) to understand constitutive models and structural micro-modelling; 4) to establish a productive dialogue with clinicians, aiming to gather the data required for model validation and offer them beneficial insights to enhance the safety of subretinal injections.
<p>Job opportunities</p>	<p>The PhD student will acquire computational and experimental skills useful for a future employment in</p> <ol style="list-style-type: none"> a) university, b) research companies, c) clinical laboratories.
<p>Composition of the research group</p>	<p>1 Full Professors 1 Associated Professors 2 Assistant Professors 1 PhD Students</p>
<p>Name of the research directors</p>	<p>Federica Boschetti, Anna Pandolfi</p>



Contacts	
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Additional support - Financial aid per PhD student per year (gross amount)	
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Housing - Foreign Students	--
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Housing - Out-of-town residents (more than 80Km out of Milano)	--
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Scholarship Increase for a period abroad	
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Amount monthly	700.0 €
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By number of months	6
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National Operational Program for Research and Innovation	
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Company where the candidate will attend the stage (name and brief description)	ASST Fatebenefratelli Sacco, Milano, https://www.asst-fbf-sacco.it/
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By number of months at the company	6
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Institution or company where the candidate will spend the period abroad (name and brief description)	School of Mathematics & Statistics of the University of Glasgow, department of Mathematics, SoftMech Group, http://www.softmech.org/
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By number of months abroad	6
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Additional information: educational activity, teaching assistantship, computer availability, desk availability, any other information

The PhD student will be hosted at LaBS and will have access to the laboratory experimental and computational facilities of the research group.

A shared desk and a PC will be given to the student for the time needed to carry out research. A limited budget will be also available for travelling and purchases.

Relevance to the theme of the call under Ministerial Decree no. 629/2024, Article 9,

Paragraph 1. The present project falls within the scope of applied research in public administrations and aims to promote greater effectiveness, efficiency, and cost-effectiveness of public action in the healthcare sector. The proposed research program falls within the disciplinary area CUN 09 - Industrial and Information Engineering. It will be carried out from a multidisciplinary perspective, developing innovative tools for computational modeling and for evaluating the effectiveness and safety of new gene therapies for the treatment of inherited retinal diseases, which may contribute to the development of specific applicative guidelines. The first gene therapy for the treatment of an inherited retinal disease was indeed approved by the Italian Medicines Agency (AIFA) in 2021. The research project will be conducted in close collaboration with the Ophthalmology Department of the Sacco Hospital (ASST Fatebenefratelli Sacco, Milan).

Institution, university, company, or research center where the period of study and research abroad will take place



School of Mathematics & Statistics of the University of Glasgow, department of Mathematics, SoftMech Group, <http://www.softmech.org/>

Months: 6

Brief description of activities: During the research period at the University of Glasgow, the doctoral student will acquire computer skills for the reprocessing of diagnostic images, learning the theoretical aspects guiding classification and comparison procedures between images, and gaining proficiency in using artificial intelligence software for subsequent stages of the thesis.

Company, research center, or public administration where the external activity will take place

ASST Fatebenefratelli Sacco, Milano, <https://www.asst-fbf-sacco.it/>

Months: 6

Brief description of activities: During the research period at Sacco Hospital, the doctoral student will become familiar with the regulatory process associated with assessing the risk of new drugs for gene therapy and with acquiring OCT images from patients and their use for numerical model validation.