UNIVERSITÀ DEGLI STUDI DI GENOVA

AREA RICERCA, TRASFERIMENTO TECNOLOGICO E TERZA MISSIONE

SERVIZIO PER IL TRASFERIMENTO TECNOLOGICO E DELLE CONOSCENZE

SETTORE VALORIZZAZIONE DELLA RICERCA, TRASFERIMENTO TECNOLOGICO E RAPPORTI CON LE IMPRESE

IL RETTORE

Vista la Legge 9 maggio 1989, n. 168 - Istituzione del Ministero dell'Università e della ricerca scientifica e tecnologica e ss.mm.ii;

Visto lo Statuto dell'Università degli Studi di Genova;

Visto il Regolamento Generale di Ateneo;

Visto il Regolamento di Ateneo per l'Amministrazione, la Finanza e la Contabilità;

VISTA la legge 7 agosto 1990, n. 241 recante "Nuove norme in materia di procedimento amministrativo e di diritto di accesso ai documenti amministrativi" pubblicata sulla Gazzetta Ufficiale n. 192 del 18/08/1990 e s.m.i.;

VISTO il Decreto del Presidente della Repubblica 28 dicembre 2000, n. 445 (Disposizioni legislative in materia di documentazione amministrativa) e s.m.i.;

VISTO il Decreto Direttoriale MUR n. 341 del 15/03/2022 di emanazione di un Avviso pubblico per la presentazione di Proposte di intervento per la creazione di "Partenariati estesi alle università, ai centri di ricerca, alle aziende per il finanziamento di progetti di ricerca di base" nell'ambito del Piano Nazionale di Ripresa e Resilienza, Missione 4 "Istruzione e ricerca" – Componente 2 "Dalla ricerca all'impresa" – Investimento 1.3, finanziato dall'Unione europea – NextGenerationEU";

VISTO il Decreto Direttoriale MUR n. 1553 dell'11/10/2022 di concessione del finanziamento del progetto Codice identificativo PE00000006, Acronimo MNESYS, Titolo "*A multiscale integrated approach to the study of the nervous system in health and disease*", registrato alla Corte dei Conti il 23/11/2022 al n. 2948 e relativi allegati;

CONSIDERATO che l'Università degli Studi di Genova è leader dello Spoke 6, dal titolo "*Neurodegeneration, trauma and stroke*";

CONSIDERATO che gli Spoke possono emanare - nell'ambito dei limiti e con le modalità previste dall'Avviso - "bandi a cascata" finalizzati alla concessione di finanziamenti a soggetti esterni per attività coerenti con il progetto approvato;

VISTA la delibera della seduta del 27 settembre 2023 con cui il Consiglio di Amministrazione dell'Università degli Studi di Genova ha approvato l'emanazione del bando a cascata per organismi di ricerca nell'ambito del Progetto MNESYS - "*A multiscale integrated approach to the study of the nervous system in health and disease* - PNRR M4C2 per lo Spoke 6;

VISTO il Decreto del Direttore Generale n. 5418 del 14 novembre 2023 di nomina del Responsabile

del Procedimento;

VISTO il Decreto del Rettore n. 5439 del 14 novembre 2023 e il Decreto Rettorale n. 5474 del 15 novembre 2023 di emanazione del Bando a cascata per il finanziamento di proposte di intervento per le attività di ricerca svolte da Organismi di Ricerca nell'ambito del programma di ricerca PE MNESYS "*A multiscale integrated approach to the study of the nervous system in health and disease*", per lo Spoke 6 dal titolo "*Neurodegeneration, trauma and stroke*", nell'ambito del PNRR, Missione 4, Componente 2, Investimento 1.3 – finanziato dall'Unione europea – NextGenerationEU (CUP D33C22001340002);

CONSIDERATO che alla data di scadenza per la presentazione delle proposte progettuali, fissata entro e non oltre il giorno 14 dicembre 2023, per la **Tematica D – "Advanced characterization of subcellular structural composition and synaptic features and their implications in neurodegenerative disorders"** era pervenuta a mezzo PEC all'indirizzo air3@pec.unige.it la seguente proposta:

PROPONENTE: Università degli Studi di Perugia
TITOLO PROPOSTA: NUMBERS – Nuclear mechanics by Brillouin elastography in intact cells mimicking laminopathy

TENUTO CONTO che la Responsabile del procedimento, Ing. Patrizia Cepollina, ha ritenuto ricevibile, ammissibile e conforme la proposta sopra citata;

CONSIDERATO che nel Bando è previsto che la valutazione di merito tecnico-scientifico dei progetti pervenuti sia affidata ad una Commissione composta da almeno tre esperti esterni al Partenariato, indipendenti e competenti dell'Area tematica dello Spoke;

VISTO il Decreto Rettorale n. 6114 del 20 dicembre 2023 con cui è stato emanato l'Avviso di manifestazione di interesse per la costituzione di un albo di esperti indipendenti a supporto della valutazione di merito dei progetti PNRR presentati sui bandi a cascata del progetto MNESYS – A multiscale integrated approach to the study of the nervous system in health and disease;

VISTO l'Estratto del Verbale della Riunione del 12 febbraio 2024 del Comitato Scientifico del programma di ricerca MNESYS "*A multiscale integrated approach to the study of the nervous system in health and disease*" che ha approvato la "Rosa di Candidati" per le Commissioni di Valutazione dei Bandi a cascata sul Programma MNESYS;

VISTO il Decreto del Rettore n. 855 del 20 febbraio 2024 con cui è costituito l'Albo a supporto delle valutazioni dei progetti presentati in risposta al bando pubblico per la selezione di proposte progettuali da finanziare nell'ambito delle attività di ricerca dello Spoke n. 6 di cui al programma di "*A multiscale integrated approach to the study of the nervous system in health and disease*" – MNESYS, a valere sulle risorse del Piano Nazionale di Ripresa e Resilienza (PNRR), Missione 4 "Istruzione e Ricerca", Componente 2 "Dalla ricerca all'impresa", linea di Investimento 1.3 "Creazione di Partenariati Estesi alle università, centri di ricerca, alle aziende per il finanziamento di progetti di ricerca di base";

VISTO il Decreto del Rettore n. 1129 del 5 marzo 2024 con cui è stata nominata la Commissione di

valutazione delle proposte pervenute in risposta al bando a cascata di cui al D.R. n. 5439 del 14 novembre 2023, indicato nelle premesse del presente decreto;

ACQUISITO il verbale della Commissione di Valutazione della seduta del 16 aprile 2024 (Prot. n. 37982 del 07/05/2024);

VISTO il Decreto del Rettore n. 2288 del 10 maggio 2024 con cui è stata approvata la graduatoria di merito per la Tematica D – "Advanced characterization of subcellular structural composition and synaptic features and their implications in neurodegenerative disorders", di cui al bando a cascata di cui al Decreto del Rettore n. 5439 del 14 novembre 2023, indicato nelle premesse del presente decreto;

TENUTO CONTO che in data 14 maggio 2024 è stata inviata all'Università degli Studi di Perugia la comunicazione con prot. n. 41381 in cui si rendevano noti gli esiti della procedura e si richiedeva la documentazione propedeutica all'adozione del provvedimento di ammissione del finanziamento;

VISTO che in data 17 maggio 2024 con prot. n. 43237 la documentazione richiesta è stata ricevuta dall'Università degli Studi di Genova che l'ha ritenuta conforme a quanto previsto nel bando a cascata di cui al Decreto del Rettore n. 5439 del 14 novembre 2023 e il Decreto Rettorale n. 5474 del 15 novembre 2023 , indicato nelle premesse del presente decreto,

DECRETA

ART. 1

L'ammissione a finanziamento del progetto NUMBERS – Nuclear mechanics by Brillouin elastography in intact cells mimicking laminopathy per la **Tematica D – "Advanced characterization of subcellular structural composition and synaptic features and their implications in neurodegenerative disorders"** con Soggetto proponente l'Università degli Studi di Perugia – come rappresentato negli Allegati B e C alla proposta presentata con domanda di partecipazione prot. n. 73926 del 12/12/2023.

ART. 2

L'entità dell'agevolazione concessa, a fondo perduto, ammonta a 150.000 euro complessivi come rappresentati nell'allegato C alla proposta presentata con domanda di partecipazione prot. n. 73926 del 12/12/2023. L'agevolazione è pari al 100% dei costi di progetto trattandosi di attività di ricerca fondamentale per Organismi di Ricerca. L'agevolazione è concessa a valere sui fondi PNRR - Programma "*A multiscale integrated approach to the study of the nervous system in health and disease*" – MNESYS Codice PE00000006 a valere sulla Missione 4, Componente 2, Investimento 1.3, ai sensi del Decreto di concessione n. 1553 dell'11 ottobre 2022, registrato alla Corte dei Conti il 23/11/2022 n. 2948, iscritto al Bilancio di Ateneo sul progetto UGOV 100009-2022-TF-PNRR-PE_MNESYS_BAC_DINOGMI.

ART. 3

Le attività, come indicate dettagliatamente nell'Allegato B alla domanda di finanziamento, dovranno essere avviate a partire dalla data di sottoscrizione del Contratto e concluse entro e non oltre 12 mesi,

affinché siano rendicontate in tempo utile per consentire la chiusura del Programma PE MNESYS, il cui termine è attualmente previsto al 31 ottobre 2025.
Potrà essere valutata e concessa una sola proroga in presenza di ritardi dovuti a circostanze eccezionali e non dipendenti da scelte del Beneficiario esclusivamente nel caso in cui il MUR, a sua volta, proroghi il termine del Programma MNESYS.

ART. 4

Il presente atto sarà pubblicato sul sito UniGe https://unige.it/progetti-finanziati-dal-pnrr e laddove la normativa vigente lo richiede.
Il documento informatico originale sottoscritto con firma digitale sarà conservato presso l'Area Ricerca, Trasferimento Tecnologico e Terza Missione.

ALLEGATI:

Allegato B – Proposta progettuale
Allegato C – Piano economico-finanziario

IL RETTORE
Prof. Federico DELFINO
(documento firmato digitalmente)

Finanziato dall'Unione europea NextGenerationEU
Ministero dell'Università e della Ricerca
Italiadomani PIANO NAZIONALE DI RIPRESA E RESILIENZA
MNESYS
Università di Genova

ANNEX B

PE00000006
"A multiscale integrated approach to the study of the nervous system in health and disease"

MNESYS

SPOKE N. 6

Research proposal

Topic addressed by the project:
d, Advanced characterization of subcellular structural composition and synaptic features and their implications in neurodegenerative disorders

NUMBERS - Nuclear mechanics by Brillouin elastography in intact cells mimicking laminopathy

- Name of the PIs' host institution for the project: Università degli Studi di Perugia
- Name of the Principal Investigators (PIs) Maurizio Mattarelli, Sabata Martino
- Proposal duration in months: 12

- Name and qualification of the Principal Investigator (PI)
- Name and qualification of the co- Principal Investigator (PI)
- Name and qualification of the components the research team

ROLE IN THE PROJECT	*NAME*	*SURNAME*	*DEPARTMENT*	*QUALIFICATION*	*YOUNG (under 40 al 31.12.2023)*	*F/M*
Principal Investigator	*Maurizio*	*Mattarelli*	*Physics and Geology*	*RTDB*		*M*
co-Principal Investigator (PI)	*Sabata*	*Martino*	*Chemistry, Biology and Biotechnology*	*PA*		*F*
	Lorena	*Urbanelli*	*Chemistry, Biology and Biotechnology*	*PA*		*F*
	Sandra	*Buratta*	*Chemistry, Biology and Biotechnology*	*RU*		*F*
	Daniele	*Fioretto*	*Physics and Geology*	*PO*		*M*
	Renzo	*Campanella*	*Physics and Geology*	*PA*		*M*

ABSTRACT

The relevance of the interplay of mechanical factors with structure and functionality in living cells is nowadays clear, and many key connections have been highlighted between mechanical alterations and the emergence of diseases at tissue as well as at single cell level. There is a growing interest to translate this concept towards pre-clinical research, but this requires a technological boost, developing reliable non-invasive tools able to characterize the viscoelastic properties of living materials with unprecedented spatial resolution. Brillouin micro-spectroscopy (BM) is recently emerging as a viable investigation method. Exploiting the light-matter interaction, it enables high-resolution optical elastography in depth inside the materials, without the use of any physical probe contacting the sample. The combination of a Brillouin spectrometer with a scanning confocal microscope proposes a new way to directly 'image' the visco-elastic properties of living matter with subcellular spatial resolution.
A significant example of diseases associated with perturbed mechanobiology functions is constituted by laminopathies, where genetic mutations alter the expression of the proteins of the nuclear lamina, in turn affecting the architecture and structural mechanics of the cell nucleus. A noteworthy instance are cells overexpressing lamin B1, the distinctive signature of autosomal dominant leukodystrophy (ADLD), a neurodegenerative laminophaty associated with a gene duplication. We plan to study for the first time by Brillouin microscopy the visco-elastic properties of in-vitro neural cell model of ADLD correlating the results with biochemical essays and fluorescence microscopy. Understanding the pathological modifications could provide a better comprehension of the molecular base of neurodegeneration in ADLD. Furthermore, the research could indicate new early diagnostic approaches based on non-invasive techniques.

RESEARCH PROPOSAL
Sections (a) and (b) should not exceed 4 pages. References do not count towards the page limits.

Section a. State-of-the-art and objectives

Mechanobiology is an emerging research field studying how cells sense and respond to mechanical cues. The cellular response to the physical stimuli generated by the extracellular matrix passes through a complex mechanism: the mechanotransducer proteins located in the plasmatic membrane activate molecular pathways collected by the cytoskeleton components and then translated to the nucleus, where a tailored gene expression program and related cell functions is activated (Argentati et al. 2019; Martino 2023; Tortorella et al. 2022; Abuwarda and Pathak 2020). The significance of such molecular pathways in the cell function, called mechanosensing and mechanotransduction processes, is highlighted by growing evidence correlating their alterations with disease development and progression (e.g., cancer, bone degeneration, brain degeneration etc.). Therefore, the elucidation of the cell mechanics may help to understand the molecular events leading the cell function in physiology and pathology.

In this regard, great attention has been devoted to the elucidation of the correlation between the mechanics of cell compartments and their function (Kim, Hah, and Wirtz 2018). In particular, the mechanics of the nucleus, the site of the DNA, generated a great amount of attention (Burridge, Monaghan-Benson, and Graham 2019; Miller, Hu, and Barker 2020). The architecture and structural mechanics of the nucleus are driven by the nuclear lamina, formed by A- and B-type lamins. Variation of nuclear stiffness has been found in laminopathies, a vast class of disorders including Emery–Dreifuss muscular dystrophy, lipodystrophy, leukodystrophy, progeria, diabetes (Ferrera et al. 2014; Apte, Stick, and Radmacher 2017; Mu et al. 2020) as well as in cancer cells (Zwerger, Ho, and Lammerding 2011; Deville and Cordes 2019; Fischer, Hayn, and Mierke 2020). Despite its great importance, the knowledge in the field of nuclear mechanics is still limited, representing a critical technical challenge: the development of new characterization strategies and sensitive techniques providing a reproducible and reliable evaluation of the mechanical properties of the nucleus is urgently needed. Atomic force microscopy (AFM) is considered the gold standard method in cell mechanics (Kirmizis 2010). However, in the study of nuclear stiffness, the AFM probe will necessarily interact with the cell membrane and with the cytosol before reaching the nucleus, giving rise to a non-trivial problem in the decoupling of the contributions given by the different cell compartments to the mechanical measurement. Brillouin micro-spectroscopy (BM) recently emerged as an innovative and alternative investigation method. Exploiting the light-matter interaction, enables high-resolution optical elastography in depth inside the materials, without the use of any physical probe contacting the sample. The combination of a Brillouin spectrometer with a scanning confocal microscope proposes a new way to directly ‘image’ the visco-elastic properties of living matter with subcellular spatial resolution. The recently developed Brillouin microscopes pave the way to new perspectives introducing a new contrast parameter in the imaging technologies. The great potentialities of the technique have not been totally explored yet and have been only recently applied to complex biological materials (Prevedel et al. 2019; Elsayad et al. 2016; Palombo and Fioretto 2019). The pioneristic investigations of single living cells indicates the technique's ability to detect the mechanical modulation of different subcellular compartments (Mattana et al. 2018; Scarcelli et al. 2015; Antonacci et al. 2018; Frittoli et al. 2023). The PI and co-PI of the project lead a multidisciplinary team combining the expertise in Brillouin imaging (Maurizio.Mattarelli-Dep. of Physics and Geology) with the deep knowledge in cells mechanobiology (Sabata.Martino – Dep. of Chem., Biol. and Biotech.). Combining these competences, the final purpose of the project is to understand the role of nuclear mechanics in laminopathies studying neural living cells. To this aim we will generate an in vitro neural cell model overexpressing the nuclear human Lamin B1. The model recapitulates the autosomal dominant leukodystrophy (ADLD) phenotype, a neurodegenerative laminopathy associated with an LMNB1 gene duplication and resulting in the Lamin B1 overexpression and nucleus alteration.

We plan to study, for the first time, the visco-elastic properties of ADLD nuclei inside living cells by the use of an innovative Brillouin-Raman microscope, moreover the effect of the Lamin B1 overexpression on the mechanotransduction pathway and on cellular communications, will be evaluated by immunofluorescence imaging and by the analysis of the secretion of extracellular vesicles. A comparative study will be performed in untransfected cells.

Understanding the pathological modifications could provide a better comprehension of the molecular basis of neurodegeneration in ADLD. Furthermore, the research could indicate new potential early diagnostic approaches based on non-invasive techniques.

The project has the following sub-objectives:

1. Generation of an in-vitro neural cell model of laminopathy

ADLD is an extremely rare disease. Therefore, to overcome the insufficiency of biological samples from human patients, we will generate an in vitro cellular model overexpressing the gene LMNB1. To better recapitulate the neurodegenerative disease, we will engineer the human glioblastoma astrocytic cell line and the human oligodendrocytic cell line MO3.13, both available commercially, according to (Ratti et al. 2021). Experiments will be performed in human embryonic kidney HEK293T cells (available in our laboratory) as reference non neural cells. If successful, the overexpression of Lamin B1 will cause abnormal Lamin B1 intermediate filaments and will alter the nuclear form.

2. Study of mechanotransduction pathways in the in-vitro neural cell model of laminopathy.

We will evaluate the effect of Lamin B1 abnormal expression on the mechanotransducer protein function. We will investigate the alteration of the Link complex, consisting of nuclear membrane proteins that allow the interaction of the nuclear lamins with the cytoskeleton fibers. The expression of focal adhesion protein will also be evaluated.

3. Characterization of extracellular vesicles in the in-vitro neural cell model of laminopathy

Due to the relevance of molecular communication between cells, we will evaluate the secretion of extracellular vesicles, which are recognized to be the vehicle of active biomolecules regulating cell functions (Théry et al. 2018). This process is also critical in the neurotransmission process, where exosomes can modulate synaptic activities rapidly by controlling neurotransmitter release or progressively by regulating neural plasticity(Xia et al. 2022). The isolated vesicles will be analyzed by spectroscopic method and biochemical assay.

4. Visco-elastic characterization of single cells and cell aggregates

The chemical and mechanical properties of the nucleus and of the relevant subcellular structures will be investigated thanks to the correlative Brillouin/Raman microscopy investigation (Scarponi et al. 2017). The evolution of the cell mechanics and nuclear mechanics will be analysed in commercially available in-vitro cellular model overexpressing the gene LMNB1- human glioblastoma astrocytic cell line and the human oligodendrocytic cell line MO3.13, as well as in human embryonic kidney HEK293T cells as reference non neural cells.

5. Multimodal Imaging Integration aided by Artificial Intelligence approaches.

Cellular complexity prevents any single technique or experiment from revealing the details of the structure and active processes. We will apply Artificial Intelligence techniques (Convolutional Neural Networks) for Multimodal Imaging Integration to combine synergically the high amount of data coming from the different microscopy techniques into a comprehensive analysis for deeply analyse the differences between wild-type and transfected cells.

6. Correlation between mechanical images and pathological state

In view of identifying new potential early diagnostic non-invasive approaches, we will investigate if it is possible to identify the pathology signature in different cells based on Brillouin micro-elastography.

Section b. Methodology

The proposed work is organized in 2 main work packages (WPs), subdivided in different tasks, which are detailed below.

WP1 generation of a neural cell model of laminopathy, mechanotransduction and vesicles secretion (WP Leader Sabata Martino)

Task 1.1. Generation of neural cell model of laminopathy (M1-M5)

U87-MG (Human glioblastoma astrocytic cell line; HTB- 14 ATCC, Virginia, US) will be cultured in Dulbecco's modified Eagle (DMEM) culture medium (Euroclone, Italy) supplemented with 10% FBS and 1% Penicillin/Streptomycin (Euroclone, Italy). Human oligodendrocyte cell line MO3.13 (Cedarlane Laboratories, Burlington, Canada) will be cultured in DMEM (Euroclone, Italy) without sodium pyruvate (Euroclone, Italy) containing % FBS and 1% Penicillin/Streptomycin. Comparative experiments will be performed in human embryonic kidney HEK293T cells (available in our laboratory). These cells will be cultured in DMEM (Corning) with 10% FBS and 1% Penicillin/Streptomycin.
Cell Transfection: the gene Homo Sapiens LMNB1 will be cloned into the pCMV6-Entry Mammalian Expression Vector. The vector pCMV6-LMNB1 will used to transfect above mentioned cells by using our procedure (Morena et al. 2017).
Wester Blotting and immunofluorescence (Morena et al. 2017) will be used to evaluate the expression of Lamin B1 and, for comparison, Lamin A.

Task. 1.2. Mechanotransduction pathway evaluations (M3-M11)

Western Blotting and immunofluorescence will be used to evaluate the expression of LINK complex (Sun and Kash proteins), cytoskeleton (F-actin and Microtubules), actin-linking proteins (Filamin, Cofilin, Myosin-II), and focal adhesion proteins (Paxillin, Talin and Vinculin), Yap and Taz proteins, and other necessary pathways according to our previous studies (Argentati et al. 2023).

Task.1.3 Vesicles secretion (M7-M11)

Culture media of transfected and control cells will be collected and used for the isolation of Extracellular Vesicles (EVs) using a differential centrifugation protocol that includes a final step of ultracentrifugation (Kowal et al. 2016; Théry et al. 2018). This protocol permits the isolation of medium/large EVs and small EVs. If necessary EVs may be isolated by size exclusion chromatography, a technique that permits the separation of vesicles according to their size.
EVs will be characterized according to guidelines reported in the Minimal Information for Studies of Extracellular Vesicles (MISEV) (Théry et al. 2018): EV morphology will be analyzed by Scanning Electron Microscopy; EV size distribution and number will be evaluated by NanoTracking Analysis; EV associated protein markers will be determined by immunoblotting.
EVs will be further characterized through the examination of lipid composition by Liquid Chromatography–Mass Spectrometry (LC-MS) and by Raman spectroscopy, a technique already employed to characterize and discriminate different EV subtypes. If necessary, the Raman signal can be enhanced by Plasmonic Resonance (Li et al. 2022). Results obtained from these experiments will be integrated, as lipid composition of EV membranes significantly influences Raman spectra.

WP2: Advanced microscopy for the viscoelastic characterization of subcellular compartments of living cells (WP Leader Maurizio Mattarelli)

Task 2.1 Correlative Brillouin/Raman spectroscopy of neural cell model of laminopathy (M3-M10)

The custom-made Brillouin microscope present in Department of Physics and Geology allows the simultaneous characterization of the molecular composition, stiffness and viscosity at the microscale using light. Using this innovative technique, we will perform a raster scan analysis with submicron spatial resolution to reconstruct the chemo-mechanical images of the cells produced in Task1.1. BM setup will be equipped with an incubator mounted on top of the inverted microscope to maintain PH and temperature of the sample constant

to 37 °C during the experiment. BM measurements will be performed for less than 2 hours in order to keep cell viability. Viability tests will be done to ensure cell viability at the end of the experiments. Moreover, since it is known that both cell nucleus and cytoskeleton organization are severely affected in the mitotic phase, cells will be analysed following serum deprivation for 24 h (quiescent cells).

Task 2.2 Artificial intelligence analysis of elastography images (M4-M12)

Laminopathies are known to affect the nuclear mechanics (Ferrera et al. 2014). The effect may regard the overall stiffness and viscosity value of the nucleus as well as their local fluctuations around the mean value, correlated with the distribution of sub nuclear components (chromatine organization, nucleoli, etc.). A simple statistical analysis of a single physical parameter is hardly able to discriminate such subtle variations. In order to gain a deeper insight, we will apply AI approaches based on CNNs to integrate the information coming from different imaging technique (bright field, Brillouin, Raman and fluorescence) utilized on the different cell types obtained in T1.1, T1.2 and T2.1. The practical steps comprise: 1) data preprocessing, to ensure consistent formats and resolutions; 2) model architecture, choosing input data, network complexity and resulting features 3) multimodal fusion, comparing early and late fusion; 4) validation and 5) identification of the most relevant features to describe the cell state.

Task 2.3 Correlation between mechanical images and pathological state (M9-M12)

This task will collect all the experimental evidence and the results of the proposed analysis of the previous tasks to correlate the presence of diseases induced in the cells with the changes in the elastography images produced by Brillouin microspectroscopy. In particular, the results obtained by biochemical assays, the morphological analysis of cells and their sub-compartments obtained by immunofluorescence and the characterization of the EV will be correlated with the innovative Brillouin microscopy images and the AI outputs. The Task aims to propose a non-invasive procedure capable of identifying early indicators of the onset of a pathology at the cellular level The proposed project not only offers new insights into laminopathies but also introduces an advanced characterization method for studying neurodegenerative disorders by analyzing modifications in cell mechanics.

WP3 Management and Dissemination (WP leader Maurizio Mattarelli)

Task 3.1. Management and Dissemination (M1-M12)

In the first month of the project an online kick-off plenary meeting will be held, inviting representatives of MNESYS -Spoke 6 to discuss the integration of NUMBERS in the major scope of MNESYS. The activities of the project will be then monitored by monthly meetings of PI and co-PI, who will oversee the day-by-day activities of the WPs, for which they are responsible. At month 6, a plenary meeting of all the participants in the project will be held to discuss development and optimize the plan of the scientific activity. A final meeting, open to anyone interested in the topic will be held at month 12 to discuss the outcome of the research. Reports of the plenary meetings will be prepared by PI and Co-PI.

NUMBERS strives to ensure effective and efficient dissemination of the project results. The PI, the co-PI and all unit members will guarantee the jointly authored publication of results in high profile biophysical, structural biology, and biophotonics journals following the Open Science and FAIR data principles. The team will disseminate NUMBERS results to scientific conferences and workshops. Moreover, according to requirement of the call, representatives of the team will participate, where requested, in meetings called by the Spoke or the HUB of MNESYS to share and discuss the development of the research.

Financial Plan:

In addition to “Personnel Cost” (49 k€), the primary budgetary allocations will stem from two research contracts (25 k€ each): one designated for a researcher specializing in cell culture and biological characterization, and the other for a researcher engaged in acquiring and analyzing spectroscopic data. Furthermore, the budget encompasses 4 k€ for mission-related expenditures and approximately 40 k€ for materials, including optics, chemicals, cell lines, and laboratory consumables.

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Vesicles and Update of the MISEV2014 Guidelines." *Journal of Extracellular Vesicles* 7 (1). https://doi.org/10.1080/20013078.2018.1535750.

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Section c. Available instrumentations and resources

High resolution Raman-Brillouin micro-spectrometer

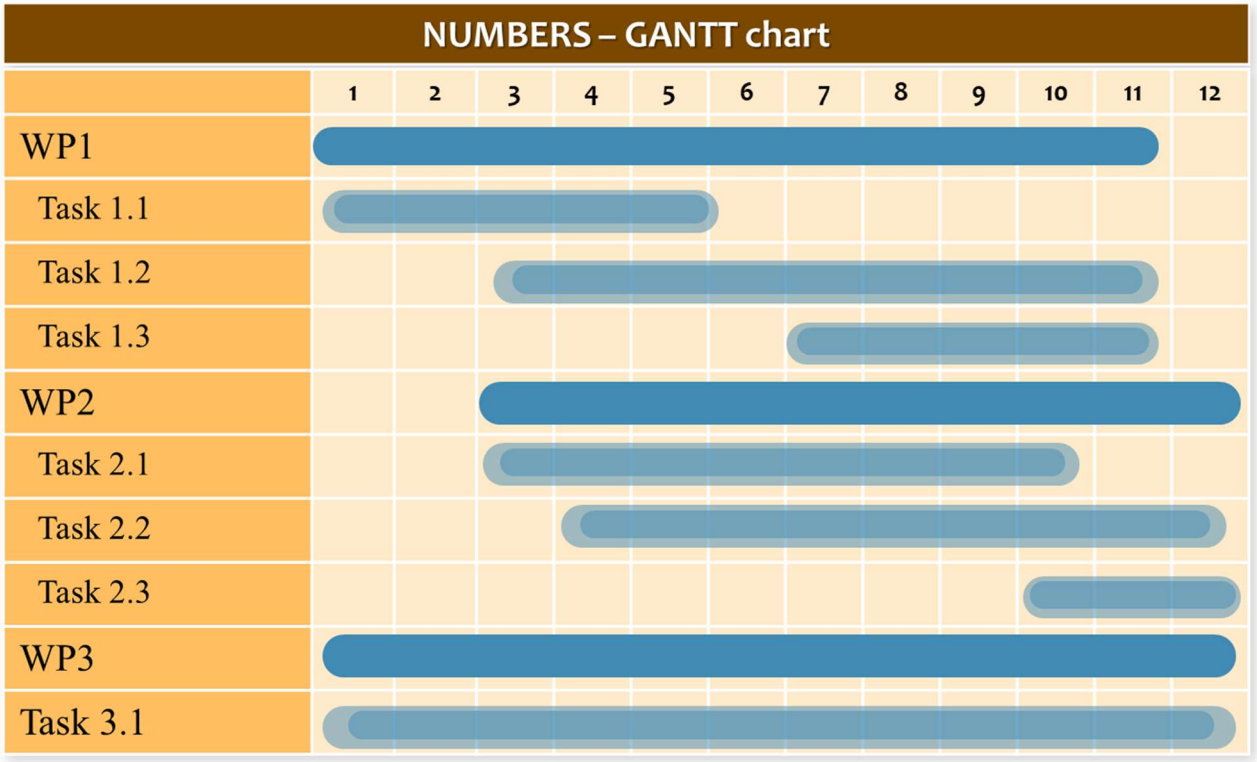
Multimodal Brillouin microscopy set up: The system was recently assembled in the UNIPG lab enabling the simultaneous detection of Brillouin and Raman light scattering signal. Our microscope combines a Raman spectrometer with a multipass Fabry-Pérot interferometer for the simultaneous characterization of morphological, chemical, and mechanical properties by all-optical investigation methods. The Brillouin interferometer has an unprecedented 150-dB contrast, which is especially important for the analysis of opaque or turbid media such as biomedical samples, and the system's spatial resolution reaches the subcellular scale. Lateral spatial optical resolution down to 500 nm. Laser source at 532 nm. The system is further equipped with OKO-LAB Stage top incubator for measurement on live cells.

Electron microscopy

FE-SEM LEO 1525 with EDX Bruker Quantax with resolution of 2.0 nm @ 30 kV equipped with AsB, InLens and SE detectors and two micromanipulators Kleindiek.

The *laboratories at the Department of Chemistry Biology and Biotechnologies* are equipped for performing biological studies with stem cells and biomaterials for tissue engineering applications, as well as for studies at molecular level (tissue culture rooms; biochemistry and molecular biology laboratories; fluorescence microscopy with video camera e software for image analyses; high-performance computing and molecular dynamics investigations; mass-spectrometric laboratory, ultracentrifuges.

Section d. GANTT diagram



Curriculum vitae Dott. Maurizio Mattarelli

PERSONAL INFORMATION

Family name, First name: Mattarelli Maurizio

Researcher unique identifiers: https://orcid.org/0000-0001-9184-7968 , Scopus Author ID: 6603348590; https://scholar.google.it/citations?hl=it&user=ew5d8UIAAAAJ;

Date of birth: 26/11/1973

Nationality: Italian

URL for web site:https://www.unipg.it/personale/maurizio.mattarelli

- **EDUCATION**

2004	PhD in Physics Department of Physics, University of Trento, Italy Supervisors: Prof. M. Montagna (Physics Department) and Dr M. Ferrari (CNR-IFN).
2002	Master Course "Materials for Information Technology and Energy Management" Istituto Universitario di Studi Superiori, Pavia, Italy.
1999	Master Sc. in Physics (Laurea Vecchio Ordinamento) Department of Physics, University of Perugia, Italy. Supervisors: Prof. L. Verdini and Prof. D. Fioretto

- **CURRENT POSITION(S)**

2021 –	Assistant Professor (RTDb) Department of Physics and Geology, University of Perugia, Italy.

- **PREVIOUS POSITIONS**

2018 – 2020	Research associate Physics and Geology Department, University of Perugia, Italy
2013 – 2018	Assistant professor (temporary position -RTDa) Physics and Geology Department, University of Perugia, Italy
2004 – 2013	Research associate Physics Department, University of Trento, Italy

- **SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS (if applicable)**

2013 – 2023	2Postdocs / 2 PhDs/ 1 Master Students Physics and Geology Department, University of Perugia, Italy
2005 – 2013	5 Master Students Physics Department, University of Trento, Italy

- **INSTITUTIONAL RESPONSIBILITIES (if applicable)**

2013 –present Faculty member, Physics and Geology Department, University of Perugia, Italy
2022 –present Member of Doctoral School in Physic, Physics and Geology Department, University of Perugia, Italy
2023 –present Member of the Joint Committee Teachers and Students for Department Teaching, Physics and Geology Department, University of Perugia, Italy

- **REVIEWING ACTIVITIES (if applicable)**

2000 –present Ad Hoc Reviewer for the following journals of applied and fundamental physics: Journal of Alloys and Compounds, Journal of Luminescence, Journal of Non-Crystalline Solids; Journal of Optics A: Pure and Applied Optics, Journal of Physics and Chemistry of Solids, Journal of Physics D: Applied Physics; Journal of Physics: Condensed Matter, European Physical Journal: Applied Physics, Material Research Bulletin; Optical Materials, Nanotechnology, Physical Review B, Physica B: Condensed Matter, Physica Status Solidi, Applied Science, Sensors, Applied Physics Letters, Light: Science & Applications..
2016 External reviewer ("rapporteur") and member of the commission for a PhD defense at the University of Lyon (France).
2016-2023 Project Reviewer for ANR (Agencie National de la Recherche), Latvian Council of Science and COST Projects
2015 –present Review Editor for Condensed Matter Physics Frontiers in Physics
2015 –present Topical Advisory Panel Member for Nanomaterials

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES (if applicable)**

2022 –present Founding Member of the "International Bio-Brillouin society" a scientific society established to advance the field of Brillouin Light Scattering as applied for life science and biomedical research and applications.
2017–2022 Member, Research Network *BioBrillouin "Brillouin Light Scattering Microspectroscopy for Biological and Biomedical Research and Applications"*

- **MAJOR COLLABORATIONS**

Prof. Claudio Canale, Cell and nuclear mechanics, Physics Department/University of Genova/ Italy
Prof. Francesca Palombo, Raman and Brillouin spectroscopy of biological matter, Physics Department/University of Exeter/UK
Dr. Edoardo Milanetto, protein aggregation in neurological diseases, Physics Department/University of Roma La Sapienza/Italy
Prof. Massimo Vassalli, mechanobiology, School of Engineering/Glasgow University/UK.

Curriculum vitae Prof.ssa Sabata Martino

PERSONAL INFORMATION

Family name, First name: Martino Sabata
Researcher unique identifier(s) (ORCID, Research ID, etc. ...): orcid=0000-0002-3942-237X
Date of birth: 16.12.1963
Nationality: Italy
URL for web site: https://www.unipg.it/personale/sabata.martino

- **EDUCATION**

1988	Master Degree in Biological Sciences. at the Department of Experimental Medicine and Biochemical Sciences, couse of Applied Biochemistry, University of Perugia (*summa cum laude*).
1989	Qualification to the Profession of Biologist. University of Perugia (DPR 980/82)
1996	PhD in "Biology, Cellular and Molecular Pathology" at University of Perugia. "

- **CURRENT POSITION(S)**

2020 -present	Director of the Biomolecular Laboratory for Recombined Proteins at CEMIN, University of Perugia.
2018-present	ITS Umbria Academy. Coordinator Academy.
2017 (Dec)-present	Associate Professor of Experimental Biology: Molecular Biology, Advanced Molecular Biology, Cell Biology. University of Perugia

- **PREVIOUS POSITIONS**

2005-2017 (nov)	**Reasercher Staff** at University of Perugia, Molecular Biology
2007-2017 (nov)	**Assistant Professo**r of Molecular Biology at University of Perugia
2017 (Dec)-present	**Associate Professor** in Experimental Biology (SSD BIO /13), University of Perugia.
2020 -present	**Director of the Biomolecular Laboratory for Recombined Proteins** at CEMIN, University of Perugia. (UNI EN ISO 9001: 2015)

- **FELLOWSHIPS AND AWARDS**

1991 (Jan)	Fellow- MURST at Division of Life Science, King's College, University of London
1997	"5th EUROPEAN AWARD ON GENE THERAPY" Associazione Malattie Rare Mauro Baschirotto).
2002	Royal Society AWARD for the project: "Directed Hexa Gene Transfer Therapy For Tay-Sachs Disease Provides A Wide Brain Distribution Of The b-Hexosaminidase A and Restores The GM2 Ganglioside Metabolism. 16-17 October, London, (UK)
2008	Prof. Luciano Belli AWARD for the work "Micropatterned hydrogenated amorphous carbon guides mesenchymal stem cells towards neuronal differentiation." (Italy)
2013	Prize "ROOTS" (IIIA Edition) granted by the City of Mesoraca (Italy)
2018	FFABR-ANVUR-Finanziamento annuale delle attività base di ricerca
2020	Nanomaterials AWARD., 20-23 January 2020, Perugia.

- **SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS (if applicable)**

2005-present	Supervisors of students (n<200) thesis of Bachelor and of Master Degree (> 70) in: Biochemistry and Laboratory of Biochemistry, Biochemical Methodology, Molecular Biology, Advanced Molecular Biology, Cell Biology (University of Perugia).
2005-present	Examining profit courses: Molecular Biology, Advanced Molecular Biology, Cell Biology.
2003-2015	Supervisors of Ph.D. students (n=5) in "Molecular Biology and Biotechnology" Ph.D. program, University of Perugia. Board Member.

2013 – present	Supervisors of Ph.D. students (n=8) in "Biotechnology" in Ph.D. program, University of Perugia. Board Member.
2022-present	Supervisors of 1Ph.D. student in the National Ph.D. program in "Photoinduced technology and processes (DIN)", University of Perugia. Board Member.

- **ORGANISATION OF SCIENTIFIC MEETINGS (if applicable)**

2007	Member of the organizing committee of the 16th European Study Group on Lysosomal Diseases (ESGLD Workshop), Perugia, Italy, September 27-30, 2007
2015-2023	Member of the organizing committee of the I, II, III, VI , V , VI, VII, VIII, IX edition of the Winter School on Biotechnology, University of Perugia.
2022	Member of the Scientific Committee of the TUM Congress, Italian Society of Biochemistry (SIB) – Tosca-Umbria-Marche. 1.12.2022 Perugia

- **INSTITUTIONAL RESPONSIBILITIES (if applicable)**

2018-present	ITS Umbria Academy. Coordinator Academy.
2015-2022 (march)	Educational Committee Member for Biotechnology at the Department of Chemistry, Biology, Biotechnology, University of Perugia. Board member.
2016-2022(march)	Quality Teaching Control Referent for Biotechnology, Department of Chemistry, Biology, Biotechnology of the University of Perugia.
2020-present	Director of the Biomolecular Laboratory for Recombined Proteins at CEMIN, University of Perugia.
2022(April)-present	President of Intercourse of Biotechnology, and of the Master's Degree Course in Molecular and Industrial Biotechnology, University of Perugia
2023(Oct)-present	Member of the Research Committee of Department of Chemistry, Biology, Biotechnology of the University of Perugia.

- **REVIEWING ACTIVITIES (if applicable)**

2018	*Guest Editor of International Journal of Molecular Science, "Cell-Biomaterial Interaction".*
2018-present	*Academic Editor of Plos ONE.*
2019-2021	Guest Editor of International Journal of Molecular Science, Special Issue "Mechanobiology in Cells and Tissues", MDPI Open Access
2019-present	Academic Editor of Journal of Personalized Medicine, MDPI Open Access
2021-present	Academic Editor of Nanomaterials, MDPI Open Access, Section "Molecular Medicine"
2014-present	Referee of PRIN and FIRB projects granted by Repubblic Italian Educational Ministry
2015-present	Referee of ELA projects
2011-2014	Member of E-Rare-2 External Advisory Board (2010-2014) - European FP7 funded project. Coordinator*GIS-Institut des Maladies Rares, Paris, FR.*
2019-present	Reviewer of ERC projects
2022	Board Member of the International Experts Panel for European National Science Center projects in Poland (Team National Science Center Foreign Member of the Expert, Poland).

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES (if applicable)**

CIB Consorzio Interuniversitario di Biotecnologie (CIB).

- **MAJOR COLLABORATIONS**

Prof. Claudio Canale, Cell and nuclear mechanics, Physics Department/University of Genova/ Italy; Prof. Francesca Palombo, Raman and Brillouin spectroscopy of biological matter, Physics Department/University of Exeter/UK; Prof. Massimo Vassalli, mechanobiology, School of Engineering/Glasgow University/UK.

Curriculum vitae Prof.ssa. Lorena Urbanelli

PERSONAL INFORMATION

Family name, First name: Urbanelli, Lorena
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Date of birth: 27th September, 1970
Nationality: Italian
URL for web site: https://www.unipg.it/personale/lorena.urbanelli

- **EDUCATION**

2001	PhD in "Molecular and Cellular Biology and Pathology" at the University of Perugia (Italy) Supervisors: Dr Paolo Monaci/Prof. Aldo Orlacchio
1995	Degree in Biological Sciences, University of Perugia (Italy), 110/110 cum laude.

- **CURRENT POSITION(S)**

2018 –current	Associate Professor of Biochemistry, Dept. of Chemistry, Biology and Biotechnology, University of Perugia (Italy)

- **PREVIOUS POSITIONS**

2018 – 2021	Assistant Professor (RTDb), Dept. of Chemistry, Biology and Biotechnology, University of Perugia (Italy)
2008 – 2018	Staff scientist, Dept. of Chemistry, Biology and Biotechnology, University of Perugia (Italy)
2007	Research associate, Dept. of Physics, University of Perugia, Italy
2005-2006	Research associate, Dept. of Experimental Medicine, University of Perugia, Italy
2001-2005	Research associate, Dept. of Biochemical Sciences and Molecular Biotechnology, University of Perugia, Italy

- **FELLOWSHIPS AND AWARDS**

25.03.2014 – 31.12.2018 Participation to the university spin-off "Enzyme & Cell Biosolutions (E&CB)" oriented to production and marketing of enzymes and micro-organisms for biotechnological applications; the spin-off won the 2012 edition of Start Cup Umbria, a competition between startups of university research, promoted by University of Perugia

- **SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS (if applicable)**

2014-2018 Co-tutor of Krizia Sagini, PhD student in Biotechnology (XXX ciclo)
2018-2022 Co-tutor of Federica Delo, PhD student in Biotechnology (XXXIV)
2019-2023 Co-tutor of Maria Grazia Cariglia, PhD student in Biotechnology (XXXV ciclo)
2021-current Co-tutor of Giada Cerrotti, PhD student in Biotechnology (XXXVII ciclo)
2022-current Co-tutor of Agnese Bertoldi, PhD student in Biotechnology (XXXVIII ciclo) in collaboration with Bios-Therapy

- **ORGANISATION OF SCIENTIFIC MEETINGS (if applicable)**

2022 Member of the Organizing Committee of TUM (Toscana Umbria Marche) 2022, a section of SIB (Società Italiana di Biochimica), Perugia, 1st December

- **INSTITUTIONAL RESPONSIBILITIES (if applicable)**

2017- Member of the Internationalization Committee of the 1st level Degree in Biotechnology, Dept. of Chemistry, Biology and Biotechnology, University of Perugia (Italy)
2023- Member of the Joint Committee Teachers and Students, Dept. of Chemistry, Biology and Biotechnology, University of Perugia (Italy)

- **REVIEWING ACTIVITIES (if applicable)**

2023- Junior Editorial Board Member of EVCNA (OAE Publishing, ISSN 2767-6641
2023- Guest Co-Editor for the Special Issue "Extracellular Vesicles and Nucleic Acids in Health and Disease" in Cells (MDPI, ISSN: 2073-4409)
2023- Guest Co-Editor of the Research Topic "Autophagy Beyond Degradation: Unraveling the Secretory Function of the Endo-lysosomal System" for Frontiers in Cell and Developmental Biology (Frontiers Media S.A., 2296-634X)
2021- Guest Editor for the Special Issue "Extracellular Vesicles as Drug Delivery Systems" for Pharmaceutics (MDPI, ISSN 1999-4923)
202- Guest Co-Editor for the Special Issue "Nucleic Acids within Extracellular Vesicles: Functional Role in Health and Disease" for Genes (MDPI, ISSN 2073-4425)
2023 Reviewer Board Member of Cells, MDPI, ISSN 2073-4409 and Pharmaceutics, MDPI, ISSN 1999-4923

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES (if applicable)**

2015- Member of ABCD (Associazione di Biologia Cellulare e del Differenziamento)
2018- Member of ISEV (International Society of Extracellular Vesicles)
2021- Member of EVITA (Extracellular Vesicles Italia, Società Italiana per le Vescicole Extracellulari)

- **MAJOR COLLABORATIONS (if applicable)**

Dr Krizia Sagini e Prof. Alicia Llorente, Department of Molecular Cell Biology, Institute for Cancer Research, Oslo University Hospital, The Norwegian Radium Hospital, 0379 Oslo, Norway

Curriculum vitae Dott.ssa Sandra Buratta

PERSONAL INFORMATION

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Date of birth: 22/06/1967
Nationality: Italian
URL for web site: https://www.unipg.it/personale/sandra.buratta

- **EDUCATION**

2002	Specialization in Clinical Pathology Department of Internal Medicine, University of Perugia, Italy Supervisor: Prof. R Mozzi
1998	PhD in Biochemical Sciences Faculty of Medicine, University of Perugia, Italy Supervisor: Prof. R. Mozzi (Faculty of Medicine)
1992	Master Sc. in Biological Sciences (Laurea Vecchio Ordinamento) Department of Cellular and Molecular Biology, University of Perugia, Italy. Supervisor: Prof. G.L. Gianfranceschi

- **CURRENT POSITION(S)**

2007 –	Researcher (RU) Department of Chemistry, Biology and Biotechnology, University of Perugia, Italy

- **PREVIOUS POSITIONS**

2004 – 2006	Researcher associate Department of Internal Medicine, University of Perugia, Italy
2002 – 2004	Researcher associate Department of Internal Medicine, University of Perugia, Italy

- **FELLOWSHIPS AND AWARDS**

2017	Grant for foreign researchers Manpei Suzuki Diabetes Foundation, Japan

- **SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS (if applicable)**

2013 – 2023	1Postdoc / 2 PhD students Department of Chemistry, Biology and Biotechnology, University of Perugia, Italy

- **ORGANISATION OF SCIENTIFIC MEETINGS (if applicable)**

2022 Member of the Organizing Committee of TUM (Toscana Umbria Marche) 2022, a section of SIB (Società Italiana di Biochimica), Perugia, 1st December

- **INSTITUTIONAL RESPONSIBILITIES (if applicable)**

2023- Member of "Commissione Orientamento", Degree in Biotechnology, Department of Chemistry, Biology and Biotechnology, University of Perugia (Italy)
2013-2019 Member of the Joint Committee Teachers and Students, Department of Chemistry, Biology and Biotechnology, University of Perugia (Italy)

- **REVIEWING ACTIVITIES (if applicable)**

2023 Guest Editor for Special Issue entitled "Proteomics and Metabolomics of Extracellular Vesicles"-Metabolites (ISSN 2218-1989).
2020 Guest Editor for Special Issue entitled "Nucleic Acids within Extracellular Vesicles: Functional Role in Health and Disease"-Genes (ISSN 2073-4425). https://www.mdpi.com/journal/genes/special_issues/extracellular_vesicles
2022 Guest Editor for Special Issue entitled "Extracellular Vesicles and Nucleic Acids in Health and Disease"-Cells (ISSN 2073-4409). https://www.mdpi.com/journal/cells/special_issues/6T7XF19VP0
2015-2019 Editorial Board Member of Neurochemical Research (ISSN 1432-1106)

2013-2023 Reviewer activities: J of Molecular Sciences (MDPI, ISSN 1422-0067); Scientific Report (Nature Research-ISSN 2045-2322); Molecules (MDPI-ISSN 1420-3049); Cells (MDPI-ISSN 2073-4409); Frontiers Physiology (Frontiers-ISSN 1664-042X)

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES (if applicable)**

2023- Member of SIB (Società Italiana di Biochimica e Biologia Molecolare)
2019- Member of EVITA (Extracellular Vesicles Italia, Società Italiana Vescicole Extracellulari)
2018- Member of ISEV (International Society of Extracellular Vesicles)
2010-2018 Member of European Society for Neurochemistry (ESN)

- **MAJOR COLLABORATIONS (if applicable)**

Dr. Carla Ferreri, Chemistry and Materials for Health and Life Sciences, ISOF, National Research Council, Bologna
Dr. Luana Lugini and Dr. Cristina Federici, Role of extracellular vesicles in cell-to-cell communication, Department of Oncology and Molecular Medicine, National Institute of Health
Dr. Lucia Catani, Role of extracellular vesicles in cell-to-cell communication, Department of Medical and Surgical Sciences, University of Bologna
Yuta Shimanaka, Lipid Biology, Department of Pharmaceutical Sciences, University of Tokyo

Curriculum vitae Prof. Daniele Fioretto

PERSONAL INFORMATION

Family name, First name: Fioretto Daniele

Researcher unique identifier(s) (such as ORCID, Research ID, etc. ...): https://orcid.org/0000-0003-4487-0035

Date of birth: 10/08/1963

Nationality: Italian

URL for web site: https://www.unipg.it/personale/daniele.fioretto

- **EDUCATION**

1994	PhD in Physics Department of Physics, University of L'Aquila, Italy Name of PhD Supervisor: Prof. Giovanni Socino
1988	Master in Physics Department of Physics, University of Perugia, Italy

- **CURRENT POSITION(S)**

2010 –	Full Professor in Physics, Department of Physics and Geology, University of Perugia - Italy

- **PREVIOUS POSITIONS**

2004 – 2010	Associate Professor Engineering Faculty of the University of Perugia - Italy
1994 – 2004	Assistant Professor Engineering Faculty of the University of Perugia - Italy

- **SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS (if applicable)**

1994 – 2023	(>10) Postdocs / (>15) PhDs/ (>20) Master Students Physics and Geology Department, University of Perugia, Italy

- **ORGANISATION OF SCIENTIFIC MEETINGS (if applicable)**

He participated in scientific and organizing committees of many conferences and schools. Recently: Chair of 2nd BioBrillouin Meeting, Perugia 12-14 September 2018; Chair of the "Winter School on Biotechnology", Perugia, January 2015-2016-2017-2018-2019-2020-2021-2022; Scientific Committee of "Confronti sulla bioetica" Università di Perugia, 3-4 dicembre 2015, Director of the school "Frontiers in Water Biophysics 2015", Erice, September 2015; member of the organizing committee of the "International Soft Matter Conference", Rome, September 2013.

- **INSTITUTIONAL RESPONSIBILITIES (if applicable)**

2004–2009 Co-founder, and member of the Governing Council of the Centre for Research and Development CNR-INFM SOFT.
2005–2010 Member of the Management Board of the University of Perugia.
2010–present Member of the Governing Council of CEMIN (Centre of Excellence on Innovative Nanostructured Materials for Physical, Chemical and Biomedical Applications).
2014–2020 Coordinator of the PhD Course on Biotechnology of the University of Perugia.
2016–2019 Vice-Director of the Department of Physics and Geology of the University of Perugia
2018¬–2021 Member of the National Committee ASN (Abilitazione Scientifica Nazionale) for the competition sector 02/B1 – Experimental Physics of Matter.
2019 – 2022 Director of the Department of Physics and Geology of the University of Perugia

- **REVIEWING ACTIVITIES (if applicable)**

He served in different international scientific panels. Among these, the Beamline Review Panel of the Electrosynchrotron ESRF and, from 2008, the Proposal Review Panel of Elettra, Trieste.
He serves as referee for several international scientific journals, including Nature, Physical Review Letters, Physical Review B, Physical Review X, Journal of Chemical Physics, Journal of Physical Chemistry, Journal of Optics, Polymer, European Polymer Journal, etc.

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES (if applicable)**

2015 – 2020 Member, European Physical Society
2014 –present Member, Società Italiana di Fisica

- **MAJOR COLLABORATIONS (if applicable)**

Nazionali:
Sincrotrone Elettra – Trieste
Istituto IPCF-CNR
Istituto ISC-CNR
Istituto IOM-CNR
Istituto di Acustica del CNR
Dipartimenti di Fisica dell'Università di Ferrara, Firenze, L'Aquila, Messina, Pisa, Roma, Trento, Laboratorio TASC e Laboratorio CSELT;
Internazionali
Sincrotrone ESRF – Grenoble
Rebirth Cluster of Excellence – Hannover
Center for Biological Physics - Arizona State University
Department of Chemistry - Colorado State University
Adam Mickiewicz University -Poznan
Max Planck Institute for Polymers – Mainz
Martin Luther Universität – Halle
Università de Rio Grande do Sul,
Exeter University (UK).

Appendix: All current grants and on-going and submitted grant applications of the PI (Funding ID)

Mandatory information (does not count towards page limits)

Current grants (Please indicate "No funding" when applicable):

Project Title	*Funding source*	*Amount (Euros)*	*Period*	*Role of the PI*	*Relation to current proposal*
CODIR	MUR (PRIN 2022)	294761 €	2023-2025	Local coordinator-(UO-UNIPG) Maurizio Mattarelli	Application of Raman-Brillouin microscopy for the characterization of protein aggregation processes
VITALITY Innovation Ecosystem	MUR (PNRR)	50000€ (Sub project)	2023-2025	PI Sabata Martino	Biomaterials and stem cells: a platform for the generation of tissue engineering
BIOforTE	MUR (PRIN 2022 PNRR)	224677 €	2023-2025	PI (UO-UNIPG) Sabata Martino	Green biomass fractionation for development of new 3D printed sustainable biocomposite materials for tissue engineering

ALLEGATO C

TABELLA COSTI PERSONALE STANDARD

FASCIA DI COSTO /LIVELLO	NUMERO SOGGETTI	COSTO ORARIO vedi nota	MONTE ORE	COSTO DEL PERSONALE
Basso	**1**	31 €	125	3'875 €
Medio	**3**	48 €	750	36'000 €
Alto	**1**	73 €	125	9'125 €
TOTALI	**5**		**1000**	**49'000 €**

COSTO ORARIO: si deve far riferimento al Decreto Interministeriale n. 116 del 24/1/2018

ALLEGATO C

BUDGET DI PROGETTO	COSTO DEL PERSONALE	OVERHEAD	Costi per servizi di Consulenza Specialistica	Costi per licenze direttamente imputabili al progetto	Costi per materiali e attrezzature direttamente imputabili al progetto	Costi per altre tipologie di spese direttamente imputabili al progetto	COSTO TOTALE
	49'000.00 €	7'350.00 €			39'650.00 €	54'000.00 €	150'000.00 €