



NANO-DAY IV

11th - 14th DECEMBER 2019

PROGRAM & BOOK OF ABSTRACTS

published with the contribution of



**UNIVERSITÀ
DI PARMA**

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ORGANIZED BY



Prof. Nelson Marmioli

*Director CINSA, Consorzio Interuniversitario Nazionale per le Scienze Ambientali
Professor Emeritus, University of Parma*



Prof. Lanfranco Masotti

President of Consorzio Italtotec



Prof. Maurizio Filippo Acciarri

University of Milano Bicocca

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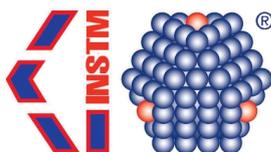
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Preface

The NANO-DAY conference series was born in Parma (Italy) in 2014 from an idea of Prof. N. Marmiroli and some of his colleagues, representing since its beginning an important meeting point for anybody interested in nanotechnology and nanoscience: academic world, research institutions and industries. Arriving to its fourth edition, the conference was moved to Milano to reach for a vaster international audience. But, the object of the conference remained the same: a platform for young researchers, and for their work. To facilitate the participation, NANO-DAY IV is completely free.

NANO-DAY IV is organized jointly by three Institutions: Consorzio Interuniversitario Nazionale per la Scienze Ambientali (CINSA) – Consorzio Italtotec – University of Milano Bicocca, hosting the event in its premises. The three components of the Organising Committee, Profs Nelson Marmiroli, Lanfranco Masotti and Maurizio Filippo Acciarri, have devised the programme of the conference with the aid of the Steering and Scientific Committees.

The event takes place from the 11th to the 14th of December 2019. In the morning of December 11th, a Round Table (in Italian) with title “Nanotechnology in Life Sciences and Technologies” will involve important representatives from institutions, academic world, industry.

The scientific programme is organized in two parallel sessions: “Life Sciences” and “Physics, Chemistry and Technology”. Each session will include four sets of oral presentations. The program will see over 70 speakers alternating on the stage. A special mention is due to the session dedicated to the Horizon2020 project SIMBA on innovations in sustainable agriculture. Speakers from Finland, Sweden, USA, India, European Commission are involved in plenary talks. There will be over 80 poster presentations organised in three sessions for discussion. The best posters and oral presentations will be selected by the Scientific Committee and awarded in the morning of December 14th, during the closure ceremony.

As a fixed feature in the NANO-DAY conferences, there will be a “job day” (December 13th) where industries, companies and spin-offs will introduce their new lines of research in the nanotechnology field. This event includes a setting where company representatives will meet young researchers.

The Organizers acknowledge the contribution of sponsors and associations providing their patronage. Moreover a more detailed list of all the people and their contribute to organization is given at page 20.

THE ORGANIZERS

Prof. Nelson Marmioli

Consorzio Interuniversitario Nazionale per le Scienze Ambientali (CINSA)
University of Parma *nelson.marmioli@unipr.it / cinsa@unipr.it*



Education and professional experience

1967-1971 degree in Biological Sciences at the University of Parma
1973-1977 Research Assistant at the University of Parma
1978 Associate Professor at the University of Chicago (IL, USA)
1979-1982 Adjunct Professor of Agricultural Genetics at the University of Udine
1980-1986 Associated Professor in Applied Genetics at the University of Parma
1986-1990 Full Professor of Genetics (Chair) at the University of Lecce
1990-1991 Chair of Genetics at the University of Bologna
1991-1995 Chair of Biology at the University of Parma
Since 1995 Chair of Recombinant DNA Technologies at the University of Parma
Since 2017 Professor Emeritus – University of Parma

Recent titles and assignments

Director of the CINSA (National Interuniversity Consortium for Environmental Sciences)
Rector Delegate and President of the Committee for University Sport Activities
He has authored over 300 scientific publications.

Milton P. Gordon Award for excellence in the career related to environmental biotechnologies (International Phytotechnology Society, 2013).

Editor of the book “Exposure to Engineered Nanomaterials in the Environment” - N. Marmioli, J.C. White, J. Song (eds). 2019, Elsevier, pp. 307-314. ISBN 978-0-12-814835-8 (doi: 10.1016/B978-0-12-814835-8.00012-1)

Main research activities

- Application of environmental biotechnologies for sustainability. Phytoremediation, bioremediation, emerging contaminants (nanomaterials and nanoparticles), interaction of plants with pollutants (outdoor and indoor).
- Genomics and proteomics of the response to environmental stress; genes and gene products involved in the adaptive response and in response to stress.
- Analysis of the effects of environmental stress and agricultural conditions on protein composition of cereal grains (durum wheat and rice), through proteomic, ionic and ultrastructural analyses. Analysis of the effects of nanoparticles of different structure on plant, fungal and animal organisms subjected to environmental stress.
- Development of molecular biosensors and nanosensors based on protein and DNA for analysis of food composition and quality; development of microsensors for on-line monitoring of food supply chains, development of *Lab-on-chip* systems. Molecular traceability in *food* and *feed*.
- Development of systems for analysis of gene expression regulation mediated by microRNAs, concerning occurrence of infective immunological and inflammatory diseases in man.
- Development of innovative tools for toxicological analyses, application to emerging contaminants and nanomaterials.
- Innovative methodologies as countermeasure against deliberate threats towards environmental and food resources.
- Production of selected plant species which can be used as natural resources to decrease the impact of conventional energy sources, using renewable resources in the production of biofuels.

Prof. Lanfranco Masotti

President of the Italbiotec Consortium for the Development of Biotechnology.
Full Professor of Biochemistry, now retired.



Career

1968-75 Assistant Professor University of Bologna, School of Medicine
1969-70 Postdoctoral Fellow A.M.A. Institute for Biomedical Research, Chicago, IL, USA.
1970-71 Assistant Professor U.A.B. Medical School, Birmingham, Alabama
1975-76 Full Professor of Medicinal Chemistry University of Catania, School of Medicine
1976-89 Full Professor of Biological Chemistry, University of Parma (UniPR), School of Medicine
1976-89 Chairman of the Institute of Biochemistry, University of Parma, School of Medicine
1976-83 Director of the School of Specialization on Biochemistry and Clinical Chemistry, UniPR
1980-86 Director of the "High Technology Instrumentation Interfaculty Center" (C.I.M.), UniPR
1983-87 Member of the Board of Directors, University of Parma, Member of the Scientific and Board of Directors of the Interuniversity Consortium for Biotechnology, Trieste
1983-89 Member of the Teaching Board of the PhD Course in Molecular Biology and Pathology, UniPR
1985-87 President of the Building Committee, Board of Directors, University of Parma
From 198 Full Professor of Biochemistry, University of Bologna, Faculty of Pharmacy
1990-2001 Director, Interdepartmental Center for Biotechnology, University of Bologna
1991-94 Member, the Academic Senate, University of Bologna
1992-98 Director, Interuniversity Consortium for Biotechnology
1992 -2010 Coordinator of the PhD Course of Cellular and Molecular Biotechnology, University of Bologna
Coordinator, School of Biotechnology, University of Bologna
1994-99 Coordinator of the Committee for the Institution of the School of Biothechnology, UniBO
1999-2010 Dean, School of Biotechnology, University of Bologna
1995-2001 Director, Department of Biochemistry, University of Bologna
1995-96 Member, Committee for the feasibility study on Structural Biology, UE-DGXII, Bruxelles
1996-99 Expert, for Biotechnology in the Central Eastern European Countries, Italian Ministry of Foreign Affairs
1997-2010 Referee, Bilateral Agreement between University of Bologna and Belgrade
1998-2003 President of the Scientific Committee and Member of the Board of Directors, Consortium for the Development of Biotechnology "Roberto Lepetit", Gerenzano (VA), Italy
1998-2010 President, Board of Governors, TESLA Scientific Center, Belgrade, YU
2000-2010 Member, Board of Governors, "Marino Golinelli" Foundation, Bologna
2000-2010 Director, Life Learning Center, Bologna
2002-2010 Member, Board of Directors, Italian Society of Biochemistry
2003-2010 Vice-President, "Marino Golinelli" Foundation, Bologna
2003-2010 President, Life Learning Center Network, Bologna
2003-2010 Manager European Federation of Biotechnology - Regional Branch Office Bologna
2003-to date President of the Consortium Italbiotech, Milano
2004-2010 Dean Corso di Laurea Specialistica in Biotecnologie Farmaceutiche
2007 -2010 Coordinator of the PhD Course of Biotecnologie, Farmacologia e Tossicologia
2007-2010 Director, Department of Biochemistry, University of Bologna

He is a Member of several scientific Societies as well of the Editorial Board of scientific Journals.
He has been coorganizer of several national and international Meetings and Advanced Courses.
He has been awarded Fellowships and has been Visiting Professor at several Universities and Research Centers in Europe, Israel, Usa, and Canada.

Number of papers in refereed journals: 162; Communications to scientific meetings: 212; Books: 4.
Research fields: Spectroscopies (CD, static and time resolved fluorescence) applied to biomolecules and biosystems. Confocal microscopy. Mass Spectrometry in Proteomics. Membrane structure and functions. Model Membranes. Liposomes as carriers of drugs and biosensors. Lipid peroxidation in tumor growth. Signalling: inhibitors of the HDACs and tyrosine kinases.

Prof. Maurizio Acciarri

University of Milano Bicocca



Maurizio Acciarri is Associate Professor in Physics at the Department of Science of the Materials of the University in Milan Bicocca.

His research activity is addressed to the study of electrical properties of semiconductors for photovoltaic application.

The research in the thin film for photovoltaic application allowed the deposition of an international patent and the technological transfer to a pilot line of the thin film deposition process of Cu(In, Ga)Se₂ for photovoltaic application.

The research in the energy sector has recently brought Maurizio Acciarri to address his interest also energy storage. In this area, he has begun a study of the capture of CO₂ from industrial fumes or biogas and its storage by conversion to methane using solar energy.

A patent has been written on CO₂ capture, and a pre-industrial prototype was developed.

Since 2004 he has been the Scientific Director of the Electronic Scanning Microscope of the University of Milano Bicocca. Since 2011 is member of the scientific committee of the Milano-Bicocca Solar Energy Research Center (MIBSOLAR) and from 2013 to 2017 he has been co-director of the centre. In 2018 he became the Director of the Centre.

Since 2014 he is member of the scientific committee and teacher for the GEM (Green Energy Management) Summer School. Since 2016 he is committee member of “BASE –Bicocca Ambiente Società Economia” at the University Milano Bicocca. Since 2017 He is member of the scientific committee and teacher for the doctorate in “SUSTAINABLE HUMAN DEVELOPMENT”. Since 2017 he is associated to the Editorial Board of the international journal Solar Energy. He is part of the Energy Working Group of the RUS (Network for the sustainable development of the Universities) as referent for UNIMIB for the Energy Sector. Since 2018, he is a member of the Technical-Scientific and Educational Committee of the Italbiotec Consortium.

Scientific Committee

Prof. Alvise Benedetti, Univ. Ca' Foscari Venezia - ITALY

Prof. Giovanni Bernardini, Univ. Insubria - ITALY

Prof. Rossella Dorati, Univ. Pavia - ITALY

Prof. Claudio Evangelisti, CNR ISTM - ITALY

Prof. Giuseppe Gallo, Univ. Palermo - ITALY

Prof. Jorge Gardea-Torresdey, Univ Texas El Paso - USA

Prof. Cristina Gonnelli, Univ. Firenze - ITALY

Prof. Arturo A. Keller, Univ. California - USA

Prof. Loredana Latterini, Univ. Perugia - ITALY

Prof. Elena Maestri, Univ. Parma – ITALY

Prof. Paride Mantecca, Univ. Milano Bicocca - ITALY

Prof. Marta Marmioli, Univ. Parma - ITALY

Prof. Monika Mortimer, UCSB Natural Reserve System - USA

Prof. Laura Polito, CNR ISTM - ITALY

Prof. Luca Prodi, Alma Mater Studiorum Univ. Bologna - ITALY

Prof. Rosaria Rinaldi, Univ. Salento - ITALY

Prof. Ana Maria Rincon, EFSA Parma - ITALY

Prof. Greta Varchi, CNR ISOF - ITALY

Prof. Jason C. White, Connecticut Agr. Experim. Station - USA

Prof. Andrea Zappettini, CNR IMEM - ITALY

Prof. Alvise Benedetti

University of Ca' Foscari, Venezia, Italy

Full Professor of Physical Chemistry. He is author of more than 150 papers published in international journals and some patents. The research has been focused on physical-chemical studies on nano particles systems (metallic and oxide), electrodes coated with thin films of oxides, catalysts, glasses and luminescent systems prepared also by microemulsions. He has been responsible for some projects supported by public and private funds. He has been Chairman of the Consortium among the University of Padua, Verona and Venezia (CIVEN) devoted to the promotion of research and training activities in the field of the nanotechnology. Past-Dean of the Faculty of Science –Università Ca' Foscari di Venezia. He is co-founder of the Center of Electron Microscopy “Giovanni Stevanato” supported by public and private funds. He is co-founder of the Heliv s.r.l., Aries s.r.l. and Nasiertech s.r.l.



Prof. Giovanni Bernardini

Dept. of Biotecnologie e Scienze della Vita, University of Insubria

Giovanni Bernardini is professor at the Dipartimento di Biotecnologie e Scienze della Vita of the University of Insubria. After having obtained his Doctor degree in Biology in 1979 at the University of Milano, he has been Postdoctoral Research Associate in the Department of Physiology of the University of Rochester, N.Y. where he studied intercellular junctions. Back to the University of Milano in 1983, he worked on gamete biology and fertilization using as a model the anuran *Xenopus laevis*. For these researches, presented at different Gordon Conferences, he collaborated with Marie Paule Cosson of the CNRS di Villefranche sM and with Jerry Hedrick of the University of California at Davis where he has been Associate in the Experimental Station in 1987. Lately, he has used *Xenopus* embryos for the development of a bioassay for evaluating the teratogenic risk. For this, in 2000 he has been invited by the Department of Health and Human Services of the U.S.A. as a member of an Expert Panel “to assess the current validation status of FETAX”. He has also been interested in gene modifications during vertebrate evolution and in functional genomics applied to animal biotechnology. Recently, he is working on nanotoxicology and bio-nano interactions with projects focusing on the direct permeation through the plasma membrane of metal nanoparticles. He is also interested in nanoparticle functionalization with antibiotics and enzymes. The research activity is documented by over 100 papers on International Journals and book chapters.



Prof. Rossella Dorati

Dept. Drug Sciences, University of Pavia, Italy

Rossella Dorati received her PhD in Pharmaceutical Chemistry and Technology at the University of Pavia (Italy) in 2006 after completing the M.Sc. in Medicinal Chemistry and Pharmaceutical Technology in 2002 from the same University. Currently, she is Assistant Professor at Department of Drug Sciences, University of Pavia. She is founder and member of the academic spin off POLYMERIX (POLYMER matRiX for life) at Technical and Scientific Park (PTS). Her research activity is mainly focused on natural and synthetic biodegradable and biocompatible polymers; parenteral micro and nano-sized carriers for controlled and targeted drug delivery; advanced topical formulations for wound healing and 3D scaffolds for regenerative medicine applications.



Prof. Claudio Evangelisti

Italian National Research Council (CNR), Institute for the Chemistry of OrganoMetallic Compounds (ICCOM), Pisa, Italy



Claudio Evangelisti in 2005 got his Ph.D. in Chemistry, University of Pisa. In 2011 he moved to Milan at the Institute of Molecular Science and Technology (ISTM) where he was scientific researcher and responsible of the electron microscopy laboratory. From 2019 he moved to Pisa where is scientific researcher at the Institute of Chemistry for the OrganoMetallic Compounds. His research activity is focused on advanced synthesis of mono- and heterometallic nanoparticles, featuring strictly controlled dimension and composition; characterization of nanostructured metal systems by Electron Microscopy characterization including electron diffraction, EDS and EELS analysis; design and development of heterogeneous catalysts.

Prof. Giuseppe Gallo

Dept. of Biological, Chemical and Pharmaceutical Sciences and Technologies - University of Palermo, Italy



Giuseppe Gallo, PhD is a Research Scientist in Microbiology at the Department of Biological, Chemical and Pharmaceutical Sciences and Technologies, University of Palermo, where he holds the course in General and Applied Microbiology in the Biotechnology degree course since 2014. He earned his PhD in Cell Biology (2004) at the University of Palermo. He is author of 35 scientific articles published on peer-reviewed journals with an H-index of 14 (Scopus) and he is also co-author of 3 scientific book chapters. His research interests cover topics related to applied microbiology and microbial biotechnology including bacterial biosynthesis and production of biomolecules of industrial and biotechnological interest, including small molecules (*e.g.* antibiotics), macromolecules (*e.g.* hydrolytic enzymes), and biogenic metal nanoparticles (*e.g.* silver nanoparticles). He has actively participated in different cooperative research projects including some involving industrial partners and European Union funded such as “Combinatorial Biosynthesis of Industrial Glycopeptides: Technology, Optimization and Production” and “LAntibiotic Production: Technology, Optimization and improved Process”.

Prof. Jorge Gardea-Torresdey

Environmental Science & Engineering, University of Texas at El Paso (UTEP)



Dr. Jorge Gardea-Torresdey is the Endowed Dudley Professor of Chemistry and Professor of Environmental Science & Engineering at The University of Texas at El Paso (UTEP). Dr. Gardea-Torresdey’s research interests include: applications of spectroscopy techniques in environmental chemistry; benefits and implications of nanotechnology in agricultural systems; development of analytical methods to detect nanomaterials; and the development of nano-enabled modular water treatment systems that are easy to deploy and that can treat and reuse challenging wastewaters. Dr. Gardea-Torresdey has a strong record of teaching and training undergraduate and graduate students. He authored over 470 publications and issued five US patents for environmental remediation. Currently, he is the UTEP PI of three major multi-institution research centers on nanotechnology: (1) the University of California Center for Environmental Implications of Nanotechnology (UC CEIN), (2) the ERC Center for Off-Grid Nanotechnology Enabled Water Treatment (NEWT), and (3) the Center to Enhance Micronutrient Use Efficiency and Increase Crop Yield using nanotechnology. The scientific contributions of Dr. Gardea-Torresdey have allowed him to receive many honors throughout his professional life such as the UTEP’s Graduate Mentor Award (2016); the 2009 SACNAS Distinguished Scientist of the Year Award; the 2012 Piper Professor Award; the distinguished 2018 University of Texas System’s STARS Retention Award.

Dr. Gardea’s career has been highlighted by the most important Journals in Science and Engineering, including Environmental Science & Technology (ES&T) and Nature. He was Editor of the Journal of Hazardous Materials from 2007 to 2010 and from 2011, he was appointed Associate Editor of ES&T.

Prof. Cristina Gonnelli

Department of Biology, UniFI, Firenze, Italy

Cristina Gonnelli got her Ph.D. in “Biology of Crop Plants”, University of Firenze in 1999. Currently she is Professor of Plant Physiology, Biology Department, University of Firenze.

Her research lines concern the study of the physiological and molecular strategies of heavy metal tolerance and accumulation in higher plants. Her favorite research models have been metallophytes of Tuscany, plants that represent also strategic biological resources in a number of emerging applications related to the remediation of metal polluted soils and waters. Recently, she has broaden her research interests to other applied issues, such as the use of plants, both wild species and crops, for the green synthesis of metal nanoparticles and liposomes of plant origin suitable for drug delivery. In addition, she has also investigated the use of lignin nano-capsules to administer protective compounds to plants.



Prof. Arturo A. Keller

University of Texas, El Paso, USA

Dr. Keller received his M.S. and Ph.D. degrees in Civil and Environmental Engineering from Stanford University. He holds a B.S. in Chemical Engineering and a B.A. in Chemistry from Cornell University. He is currently a Professor at the University of California in Santa Barbara, teaching at the graduate-level Bren School of Environmental Science and Management. He has published over 230 peer-reviewed papers. Dr. Keller is co-Director of the NSF and USEPA funded UC Center for the Environmental Implications of Nanotechnology (CEIN), funded for 10 years for a total of \$48M, which is dedicated to providing key information for addressing and managing any risks that may arise during the use of nanotechnology. Dr. Keller leads the group studying fate & transport, exposure and life cycle assessment of nanomaterials and other emerging contaminants. In recognition of his contributions in this area, in 2015 Dr. Keller received the Agilent Thought Leadership award (\$1.5M).

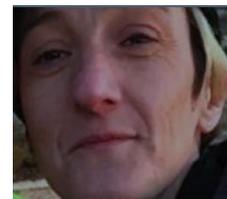
Dr. Keller is also a co-Director of the USEPA funded Chemical Life Cycle Collaborative, which seeks to develop a framework to make early predictions of the life-cycle implications of a new chemical or material, based on the chemical structure, applications and use characteristics.

Prof. Loredana Latterini

Department of Chemistry University of Perugia, Italy

Loredana Latterini, is full professor of Physical Chemistry at the University of Perugia (03/A2-SSD CHIM/02). Prof. Latterini has promoted and established in the department of Chemistry of Perugia the research topics concerning nano-structured materials responsive to electromagnetic radiation. Prof. Latterini's group has developed the abilities to use nanotechnology procedures (bottom-up strategies) to prepare nanomaterials with optical and electronic properties determined by size and morphology and a functional surface chemistry.

Recently, prof. Latterini has been appointed as PI of the laboratory *Nano4Light* included in the AMIS Project - funded by MIUR through the Excellent Departments program 2018-2022.



Prof. Elena Maestri

**Dept. Chemistry, Life Sciences and Environmental Sustainability, UniPR,
Parma, Italy**



Elena Maestri has a degree in Biology and a PhD in Genetics. She is Full Professor of Applied Biology at the University of Parma, in the Department of Chemistry, Life Sciences, and Environmental Sustainability. She is the President of the Degree in Biotechnology and member of the PhD Course in Biotechnology and Life Sciences. Her teaching activities cover Cell and Animal Biology, Environmental Biology, Applications of Transgenic Organisms. The research activities are focused on two main topics:

- sustainable agriculture in the framework of circular economy
- environmental biotechnologies, phytoremediation, effects of pollutants including nanoparticles as emerging contaminants.

She authored over 250 publications. She is in the Editorial Board of the journals 'Environmental Science and Pollution Research' and 'International Journal of Phytoremediation'.

Prof. Paride Mantecca

**University of Milano-Bicocca, Department of Earth and Environmental
Sciences**



Paride Mantecca, Associate professor of Comparative Anatomy and Cytology at the University of Milano-Bicocca, Department of Earth and Environmental Sciences. Director of the Research Center POLARIS (Particulate Matter and Health Risk), University of Milano-Bicocca. PM dedicated his research activities to the following fields: i) studies on the reproductive and developmental patterns of invertebrate and vertebrate, with major attention to the perturbations induced by environmental pollutants; ii) biological effects of particulate matter (PM10, PM2.5, wear and combustion-derived particles on in vitro and in vivo systems; iii) nanotoxicology and nanosafety, with particular emphasis on the bio-nano-interactions occurring between engineered nano-biocidals (e.g. antimicrobials) and cells and tissues of the main biological barriers (lung and intestine), contributing to a safe-by-design approach of nanotechnologies.

PM coordinates and collaborates in national and international projects in the field of Particulate Matter toxicity, nanotoxicology and nanosafety. PM is responsible of Cell and Developmental biology labs, environmental toxicology labs, histology and electron microscopy labs.

Prof. Marta Marmiroli

Dept. Chemistry, Life Sciences and Environmental Sustainability, UniPR, Parma, IT

BSc (Hons) in Solid State Physics, Parma University. PhD in Biotechnology, Parma University, "Applications of scanning electron microscopy, microanalysis, micro-fluorescence and EXAFS to environmental biotechnology". OECD grant for research on N use in agriculture. Associate Professor at Parma University, Lecturer in Applied Biotechnology and Phytoremediation. Research focus on food security in several EU and NATO projects. Collaboration with Canterbury and Lincoln University, NZ; CAES (The Connecticut Agricultural Experiment Station, CT., USA); The James Hutton Institute (UK); The Harper Adams University (UK), ELETTRA synchrotron, Trieste, other synchrotrons: ESRF Grenoble (France), DASY Hamburg (DE). Main interest in investigation of plant/yeast-metals /ENMs interaction through advanced "-omics", microscopy, EDX, and synchrotron-light based methods.

Prof. Monika Mortimer

Institute of Environmental and Health Sciences, College of Quality and Safety Engineering, China Jiliang University, Hangzhou, Zhejiang, China



Dr. Monika Mortimer is an Associate Professor in the Institute of Environmental and Health Sciences at China Jiliang University, Hangzhou, Zhejiang, China. Dr. Mortimer received her Ph.D. in Chemistry from Tallinn University of Technology, Estonia. She was a postdoctoral fellow at the University of Geneva, Switzerland in 2012-2013 and at the University of California, Santa Barbara (UCSB) and the UC Center for Environmental Implications of Nanotechnology (UC CEIN) in 2014-2016. She continued her appointment with UCSB as a Project Scientist in 2016-2019. Dr. Mortimer's research focuses on environmental and health impacts of engineered nanomaterials. Her areas of expertise include microbiology, molecular toxicology, nanomaterials, and environmental fate and effects of chemicals. Her recent interests include transcriptomics to elucidate the mechanisms of action of nanomaterials in microorganisms that play crucial roles in human health and agriculture. She has published over 40 peer-reviewed articles, including six critical reviews and one perspective, in high-impact journals such as ACS Nano, Environmental Science & Technology and Environmental Science: Nano on the toxicity and environmental impacts of engineered nanomaterials. Dr. Mortimer serves as an Academic Editor of PeerJ and as a guest editor of Nanomaterials special issue "Advances in Nanotoxicology".

Prof. Laura Polito

Institute of Science and Chemical Technologies "G. Natta"- SCITEC-CNR, Milano, Italy



Laura Polito got her Ph.D. in Chemical Science in 2006 from the University of Milan (IT). After 2 years of post-doc at the University of Milan working on the synthesis of saccharide-based antigen and their polyvalent conjugated for improving immunity system, she joined the Institute of Molecular Science and Technologies of the Italian National Research Council (CNR). Currently, she is Research Scientist at the Institute of Science and Chemical Technologies "G. Natta"- SCITEC-CNR. Her research activity is mainly focused on the synthesis and functionalization of smart nanoparticles and their use in biomedical field; the development of microfluidic-based protocols for the synthesis of metal nanoparticles; the synthesis and application of hybrid nanomaterials to obtain complex nanostructures with attractive applications in biomedical, sensing and catalytic field; the manipulation and engineering of glycan-based nanosystems.

Prof. Luca Prodi

University of Bologna



Luca Prodi received its Ph.D. Degree in Chemistry in 1992 at the University of Bologna. In 1991 he was visiting scientist at Argonne National Laboratory (IL, USA) under the supervision of Prof. Michael Wasielewski. He was appointed as Full Professor of General and Inorganic Chemistry at the University of Bologna in 2006, and has been Head of the Department of Chemistry "Giacomo Ciamician" from 2015 to 2018. In 2012 it was invited Professor at the École Normale Supérieure de Cachan, France. His research activity is focussed on the synthesis and characterization of photoactive silica nanoparticles for application in nanomedicine. Prof. Prodi is author or co-author of more than 215 articles published on peer reviewed international journals, inventor in 7 Italian patents and 4 PCT extensions, and is co-founder of two spin-off companies; his h-index is 58 (Scopus and WoS). In 1990 Prof. Prodi received an important award from Federchimica (Association of the Italian chemical companies), and in 2009 the Gonzales-Ciamician prize, awarded by Real Sociedad Española de Química.

Prof. Rosaria Rinaldi

Dept. of Mathematics and Physics "Ennio De Giorgi" of the University of Salento



Rosaria Rinaldi is Full Professor of Physics of Matter at the Department of Mathematics and Physics "Ennio De Giorgi" of the University of Salento. She is director of the Laboratory of "Interdisciplinary Applications of Exact Sciences" and a member of the Executive Council of the University School of Excellence "ISUFI High School" (University Institute for Interdisciplinary Education) of the University of Salento. She is coordinator of the PhD course in Physics and Nanosciences and directs the Regional Laboratory "Nano-Biotechnologies for the Diagnosis and Development of Innovative Therapies - NaBiDiT". The professor is a member of the working group on the promotion of the SCIENTIFIC PROJECTS & ACTIVITIES of the University of Salento. R. Rinaldi is author and co-author of more than 280 articles published in peer reviewed international journals, about 13 monographs and of 11 patents, with a Citation Index of 35 (THOMSON REUTERS-WEB OF KNOWLEDGE). Professor Rinaldi is the head of the Nanomedicine, Nanobioelectronics e and Nanobiotechnology Laboratory of Unisalento, where she coordinates the research activity of an interdisciplinary research group of 25 scientist, including young researchers, post-doc and Ph-D students. The Nanomedicine, Nanobioelectronics e and Nanobiotechnology Laboratory is a joint lab of the Dept. of Mathematics and Physics of UNISALENTO and of CNR-IMM in Lecce. The Lab consists of a cross-disciplinary NanoTechnology and NanoScience facility for nm-scale research and technology applied to lifescience, medicine, and food and environment safety.

Prof. Ana Maria Rincon

European Food Safety Authority (EFSA), Parma, Italy



Dr Ana M Rincon has been a Scientific Officer of the Food Ingredients and Packaging (FIP) Unit of the EFSA for more than ten years. She has a strong knowledge on risk assessment, EU food law and EU regulatory framework. In her role in EFSA, she coordinates working groups of the EFSA Panel on Food Additives and Flavourings (FAF) dealing with the re-evaluation of food additives or the evaluation of substances to be authorised as food additives in the EU. Dr Rincon holds a PhD in the area of supramolecular chemistry from the Universidad Autonoma de Madrid. She has peer-reviewed papers in various areas of chemistry related research and contributed to several EFSA opinions. In the last years she has been involved in the risk assessment of substances containing nanoparticles.

Prof. Greta Varchi

CNR ISOF, Italy



Dr. Greta Varchi graduated in Industrial Chemistry at the University of Bologna in July 1997. Later, she spent 6 months as visiting researcher at the Dep. of Organic Chemistry at the Fachbereich Chemie of the University of Marburg (Germany). She received her Ph.D. in Chemical Sciences from the University of Bologna (Italy) in 2001, during which she spent 6 months at the Dep. of Chemistry at the LMU of Munich (Germany). In 2002 she achieved the position of researcher at the Institute of Organic Synthesis and Photoreactivity (CNR, Bologna) and from 2003 till 2004 she was postdoctoral fellow at the Department of Organic Chemistry at the Stony Brook University (NY, USA). In 2017 she was appointed as Full Affiliate Member at the Department of Nanomedicine at the Houston Methodist Research Institute (Houston, Texas, USA). Greta is author of more than 90 scientific contributions in peer-reviewed journals, 3 book chapters and 5 patents. She is coordinator/collaborator of several national research projects and she serves as associate editor of *Frontiers in Organic Chemistry*, as peer reviewer of numerous scientific journals and as an expert evaluator for the European Commission.

Prof. Jason C. White

Connecticut Agr. Experim. Station – USA

I am currently Vice Director of the Connecticut Agricultural Experiment Station, as well as Head of the Department of Analytical Chemistry. I am also State Chemist. I received a B.S. in Ecology from Juniata College in Huntingdon, PA in 1992. I received my Ph.D. in Environmental Toxicology from Cornell University in 1997. I did a one-year post-doctoral position at the Connecticut Agricultural Experiment Station in New Haven CT from 1997-1998 in the Department of Soil and Water. I am a Visiting Scientist within the Harvard University TH Chan School of Public Health. I also have adjunct status at the University of Texas-El Paso, University of Massachusetts, and Post University. I am Managing Editor for the International Journal of Phytoremediation, Immediate Past President of the International Phytotechnology Society, on the Editorial Advisory Board (SAB) of Environmental Science and Technology and Environmental Science and Technology Letters, and on the editorial boards of Environmental Pollution and NanoImpact. My h-index is 54; I have published about 200 papers and my work has been cited 9,212 times. My primary research interests include nano-enabled agriculture, nanotoxicology, and food safety.



Prof. Andrea Zappettini

CNR IMEM, Italy

Andrea Zappettini got a degree in Physics and a master in Material Science at the University of Parma. After working for Eni and Pirelli, he became researcher at Istituto Materiali for Elettronica e Magnetismo (IMEM), an Institute of the Italian National Research Council (CNR). Since 2019 he is director of IMEM. His research activity has been mainly devoted to the development of sensors based on novel and multifunctional materials.



THE STEERING COMMITTEE

Dott. Diego Bosco, Consorzio Italbiotec Milano - ITALY

Dott.ssa Silvia Lepore, Consorzio Italbiotec Milano - ITALY

Prof. Elena Maestri, Università di Parma - ITALY

Prof. Laura Polito, CNR ISTM – ITALY

The Organizers want to thank also:

Dott.ssa Laura Paesano, CINSA Parma - ITALY

Dott. Davide Imperiale, SSICA Parma - ITALY

Dott.ssa Francesca Mussi, Università di Parma - ITALY

Dott. Luca Pagano, Università di Parma - ITALY

Dott.ssa Marina Caldara, Università di Parma - ITALY

Dott.ssa Valentina Gallo, Università di Parma - ITALY

Dott.ssa Roberta Ruotolo, Università di Parma - ITALY

Dott.ssa Sara Graziano, Università di Parma - ITALY

Dott. Riccardo Rossi, Università di Parma - ITALY

Dott.ssa Urbana Bonas, Università di Parma - ITALY

Dott.ssa Nadia Palermo, Università di Parma - ITALY

their availability and dedication has been fundamental to the organization of the meeting.

Programme

Wednesday, 11 December	
08:30	Welcome coffee and REGISTRATION
09:30	Opening of the Conference – Welcome <i>Prof Filippo Maurizio Acciarri</i> - Univ. Milano Bicocca <i>Prof. Giovanna Iannantuoni</i> - Rector - Univ. Milano Bicocca <i>Prof. Lanfranco Masotti</i> - Consorzio Italtotec <i>Prof. Nelson Marmioli</i> - Consorzio Interuniversitario Nazionale per le Scienze Ambientali
10:00	Round Table “Nanotechnologies in Life Sciences and Technology” – “Nanotecnologie nelle Scienze della Vita e nelle Tecnologie”
	Round Table Director <i>Vittoriano Zanolli</i> , La Provincia di Cremona newspaper Speakers <i>Attilio Fontana</i> , Presidente Regione Lombardia <i>Flavia Barone</i> , Istituto Superiore Sanità <i>Mario Bonaccorso</i> , ASSOBIOTEC-FEDERCHIMICA <i>Andrea Caneschi</i> , Direttore Consorzio INSTM <i>Dario Dalla Vedova</i> , CONI <i>Cristina Leone</i> , Gruppo Leonardo (Finmeccanica)
12:00	Lunch break
14:20	Introduction to Sessions A and B (Aula 1)
14:30	Plenary Lecture: <i>Leo Miglio</i> (Univ. Milano Bicocca) – From Science to Technology
Parallel Session 1A - “Nanotechnologies and nanomaterials in agriculture and food production” (in association with SIMBA H2020 project)	
15:10	Mini Plenary Lecture: <i>Anne Pihlanto</i> (LUKE, Finland) - Sustainable innovation of microbiome applications in the food system
15:40	<i>Silvia Tabacchioni</i> (ENEA, Roma) - Design of microbial consortia with plant growth-promoting activity for sustainable crop production
16:00	<i>Minna Kahala</i> (LUKE, Finland) - Microbial processing for nutritional enhancement of plant based products
16:20	<i>Anne-Maria Pajari</i> (Univ. Helsinki, Finland) - Sustainable foods and human gut microbiota
16:40	Coffee break
17:00	<i>Milena Stefanova</i> (ENEA, Bologna) - Sustainability Assessment and Potential Uptake of Innovations
17:20	<i>Riccardo Rossi</i> (Univ. Parma) - Effects of Copper Oxide nanomaterial on plant flowering: a transcriptomic and physiological approach to enable sustainable food production
17:35	<i>Gregorio Dal Sasso</i> (CNR IC, Como) - Nitrate-doped Biomimetic Calcium Phosphate Nanoparticles as N and P Slow-Release Nanofertilizers via Particle Dissolution
17:50	<i>Andrea Ciurli</i> (Univ. Verona) - FePO ₄ nanoparticles as a source of nutrients: effects on plant transcriptome and on soil microbial communities and functions
Parallel Session 2A - “New materials for nanotechnologies” (synthesis, testing, characterisation)	
15:10	Mini Plenary Lecture: <i>Michele Iafisco</i> (CNR ISTECC, Faenza) - Tailoring the chemistry of bioceramic nanoparticles for unconventional applications
15:40	<i>Valentina Palmieri</i> (Univ. Catt, Sacro Cuore, Roma) - Laser Patterning of Graphene Oxide induce bone regeneration
16:00	<i>Emanuele Longo</i> (CNR IMM, Agrate Brianza) - ALD growth of Co thin films on the topological insulator Sb ₂ Te ₃
16:20	<i>Tommaso Giovannini</i> (NUST, Norway) - A novel classical approach to optical properties of metal nanoparticles
16:40	Coffee break
17:00	<i>Margaux Bouzin</i> (Univ. Milano Bicocca) - Nanoparticles Localization in Tissues at Sub-Diffraction Level by Infrared Thermal Imaging
17:15	<i>Artur Tuktamyshev</i> (Univ. Milano Bicocca) - Telecom InAs QDs grown by Droplet Epitaxy on vicinal GaAs(111)A
17:30	<i>Marcello Marelli</i> (CNR SCITEC, Milano) - In-flow Synthesis of Multibranched Au/TiO ₂ Hybrid

	Nanosystem: Exploiting the Plasmonic Features for Catalytic Purposes
17:45	Anna Maria Ferretti (CNR SCITEC, Milano) - Synthesis, characterization and application of low band gap rod-coil block copolymer water-processable nanoparticles, synthesized by surfactant-free miniemulsion approach
18:00 18:30	Poster Session A

Thursday, 12 December	
8:30	Plenary Lecture: <i>Bengt Fadeel (Karolinska Inst., Sweden)</i> - Nanotoxicology: focus on the impact metal and metal oxide nanoparticles
Parallel Session 1B - “Nanotechnologies and nanomaterials for human and animal health” (pharmaceutical and medical applications)	
9:10	Mini Plenary Lecture: <i>De Angelis (ISS, Roma)</i> - Towards the Risk Governance of Nanotechnologies: the ISS Multidisciplinary Unit
9:40	Lucia Gemma Delogu (Univ. Padova) - Immune characterization of graphene-based materials for the design of new tools in biomedicine
10:00	Lucia Paolini (Univ. Brescia) - Exploiting blood nanoparticles for augmented pathogenesis identification
10:20	Giordano Perini (Univ. Catt. Sacro Cuore, Roma) - Graphene Quantum Dots for the Treatment of Glioblastoma Multiforme
10:40	Coffee break
11:00	Arianna Rossetti (Polit. Milano) - Selective modulation of A1 astrocytes by drug-loaded nanostructured gels in spinal cord injury
11:15	Silvana Fiorito (CNR ITP, Roma) - Neuroprotective effect of Metallic Multi Walled Carbon Nanotubes
11:30	Eleonora Terreni (Univ. Pisa) - Mucoadhesive polymeric inserts containing Cyclosporine-A loaded nanomicelles for the treatment of dry eye syndrome: technological and biopharmaceutical characterization
11:45	Rossella Bengalli (Univ. Milano Bicocca) - In vitro toxicity of antibacterial metal oxide nanoparticles: effects on 2D and 3D skin and lung models
Parallel Session 2B - “Sensors from nanotechnologies and new nanomaterials”	
9:10	Mini Plenary Lecture: <i>Nicola Coppedè (CNR IMEM, Parma)</i> Integrated and distributed sensors for the IOT
9:40	Stefano Stassi (Polit. Torino) - Nanomechanical resonators from suspended DNA fibers for structural analysis
10:00	Daniele Moscheni (CNR IC, Como) - The Role of Advanced X-ray Scattering Techniques on Nanomaterials Characterization: A case study on CdSe-based Colloidal Quantum Dots
10:20	Laura Riva (Polit. Milano) - Aromatic Imides Functionalized Cellulose Nanosponges for Naked-Eye Heterogeneous Sensing of Fluoride
10:40	Coffee break
11:00	Lucia Ganzer (Polit. Milano) - Tailoring optical properties and stimulated emission in nanostructured polythiophene
11:15	Federico Polo (Univ. Ca' Foscari, Venezia) - Perspectives on Nanostructured Architectures for Biosensing Applications and New Analytical Tools: Toward Precision Medicine
11:30	Francesca Berini (Univ. Insubria) - Magnetic nanoconjugated glycopeptides as novel tools for bacterial infection site targeting

11:45	Cecilia Martini (CNR ISOF, Bologna) - Intercalation of Bioactive Molecules into Nanosized ZnAl Hydroxalicates for Combined Chemo and Photo Cancer Treatment
12:00 14:30	Lunch break and posters
14:30	Plenary Lecture: Davide Prosperi (Univ. Milano Bicocca) - Critical issues in the clinical translation of nanobiotechnology research and future directions of nanomedicine
Parallel Session 1C - "Nanotechnologies and nanomaterials for different environments" (risk assessment, monitoring and remediation)	
15:10	Mini Plenary Lecture: Om Parkash Dhankher (University of Massachusetts, USA) - Toxicity of Metal-Based Engineered Nanoparticles in Crops and Their Impact on Global Food Security and Safety
15:40	Massimiliano Bianchi (Univ. Parma) - Amorphous silica nanoparticles interfere with LPS-dependent metabolic changes in human macrophages
16:00	Davide Fissore (Polit. Torino) - Use of chitosan nanoparticle to vehicle dsRNAs against tomato spotted wilt virus in plants
16:20	Andrea Fiorati (Polit. Milano) - Eco-design of nanostructured cellulose sponges for sea-water decontamination from heavy metal ions
16:40	Coffee break
17:00	Stefano Rossi (Univ. Parma) - Direct effects of diesel exhaust particles on different cell lines as well as on in vivo rat heart: Euro III vs. Euro IV engines
17:15	Tiziana Silveti (CNR ISPA, Milano) - Chemo-enzymatic oxidation of plant galactomannans with laccase/TEMPO for production of renewable biomaterials, also as delivery systems
17:30	Stefania Federici (Univ. Brescia) - Reference Materials for Environmental Nanoplastic Pollution
17:45	Luca Pagano (Univ. Parma) - Maintenance and expression of organelle information in plants exposed to engineered nanomaterials
Parallel Session 2C - "New industrial processes and products based on nanotechnologies and nanomaterials" (including new energy sources)	
15:10	Mini Plenary Lecture: Agnieszka Mech (European Commission) – Regulatory aspects of nanomaterials issue: towards safe, sustainable and responsible innovation
15:40	Enrica Chiesa (Univ. Pavia) - Development of a rapid and low-cost microfluidic process enabling efficacious and specific CD44 targeted delivery by using HA-based nanoparticles
16:00	Matteo Zaffalon (Univ. Milano Bicocca) - Evidence for the Band-Edge Exciton of CuInS ₂ Nanocrystals Enables Record Efficient Large-Area Luminescent Solar Concentrators
16:20	Roberto Sorrentino (CNR SCITEC, Milano) - Nanoplatelets Light Emitting Diodes with tunable cathode and anode interfaces properties
16:40	Coffee break
17:00	Silvia Mostoni (Univ. Milano Bicocca) - Nanosized and single site zinc-based activators for reducing ZnO in rubber vulcanization process
17:15	Alberto Vomiero (Univ. Ca' Foscari Venezia) - Interfacial properties in composite nano-systems for energy harvesting
17:30	Jessica Gasparello (Univ. Ferrara) - Validation of a novel argininocalix[4]arene macrocycle as transfection agent for miRNA-mimicking and anti-miRNA molecules

17:45	Francesca Carella (CNR ISTECC, Faenza) - From food industry by-product to a novel UV filters production for sunscreen applications
18:00 18:30	Poster Session B

Friday, 13 December	
8:30	Plenary Lecture: Arturo Keller (Univ. California, USA) - Elucidating crop plant response to engineered nanomaterials using metabolomics and proteomics
Parallel Session 1D - "Nanotechnologies and nanomaterials to expand biotechnology and promote business" (industrial nanobiotechnology and marketing its products)	
9:10	Mini Plenary Lecture: Jason C. White (CAES, USA) - Nanotechnology in agriculture: Balancing applications and implications
9:40	Cristina Caffarra (Univ. Parma) A 3D bioprinted model for in vitro nanotoxicological investigation: preliminary studies
10:00	Denise Beconcini (Univ. Siena) Nanoparticles based on chitosan-derivatives as delivery systems for natural cherry extract polyphenols
10:20	Francesco Gentile (Univ. Federico II Napoli) Superclusters of neuronal cells on zinc oxide nanowires surfaces
10:40	Coffee break
11:00	Andrea Perrelli (Univ. Torino) Development of combinatorial targeted therapeutic strategies based on nanotechnology for Cerebral Cavernous Malformation disease treatment
11:15	Patrizia Cancemi (Univ. Palermo) Biogenerated Silver nanoparticles: promising antitumoral drugs for cancer therapy
11:30	Elena Bossi (Univ. Insubria) To cross or not to cross: some, but not all, metal nanoparticles enter cells by plasma membrane direct crossing
11:45	Valentina Gallo (Univ. Parma) - Protein responses in eukaryotic cells exposed to cadmium sulphide quantum dots
Parallel Session 2D - "Safer nanotechnologies and nanomaterials for the future" (planning, using, safe by design, marketing safer nanotechnologies)	
9:40	Parisa Fatehbasharzarad (Univ. Torino) - Engineering Shape of Nanoparticle-Based Magnetic Resonance Imaging Contrast Agent
10:00	Valentina Bello (Univ. Pavia) - Micro-capillary refractive index sensor based on monitoring of T/R ratio spectral shift
10:20	Ruben Foresti (Univ. Parma) - 5D printing nano-laden scaffold for personalized medicine
10:40	Coffee break
11:00	Valerio Pinchetti (Univ. Milano Bicocca) - Dual emitting CdSe/CdS nanocrystals hosting core-and shell-based excitons for last-generation nanotechnologies and as platform for fundamental investigations
11:15	Vittoria Viganò (Univ. Insubria) - Nanomedicine: is there plenty of room for ethics?
11:30	Stefania Gottardo (JRC, Ispra) - Quality and completeness of physicochemical data for safety assessment of nanomaterials
11:45	Marcello Berto (Univ. Modena Reggio Emilia) - Carbon nanotubes/proteins hybrid for Organic Electronics
12:00	Mini Plenary Lecture: Luca Prodi (Univ. Bologna) - Dye Doped Silica Nanoparticles as Organized Systems for Nanomedicine
12:30	Lunch break
12:30 14:00	Poster Session C

Job Day “Where Industry meets with researchers”	
14:00	Presentations from Companies of Nano sector - selected abstracts
14:00	Marek Atanasčev (CzechTrade, Czech Republic) - Introduction
14:15	Luca Gentilucci (Univ. Bologna) - Diagnostic and theranostic implementation of dye-loaded peptide-functionalized inorganic nanoparticles targeting integrin-expressing cells
14:25	Davide Segà (Univ. Verona– Fabbrica Cooperativa Perfosfati Cerea) - FePO ₄ nanoparticles produced by an industrially scalable continuous-flow method are an available form of P and Fe for cucumber and maize plants
14:35	Eride Quarta (Univ. Parma– PlumeStars srl) - Microparticles Embedding CaP Nanoparticles for Heart Targeting by Inhalation: Quality by Design Approach for Dry Powder Inhaler Composition
14:45	Silvia Pisani (Policlinico S. Matteo, Pavia – Polymerix Srl) - Release of IL-8 from BXPC-3 pancreatic tumor cells influenced by nanostructures
14:55	Filippo Vurro (CNR IMEM – Mutti SpA) - Addressing water scarcity in agriculture: the new frontiers of the in vivo monitoring in open field tomato cultivation
15:05	Alessandra Ronchi (Univ. Milano Bicocca– Glass to Power SpA) - Triplet fusion-based hybrid upconverters: achieving 100% triplet sensitization yield by charge-engineered semiconductor nanocrystals
15:15	Giuseppe De Giorgio (Univ. Parma) - Toxicological assessment of food-grade nanoparticles
15:30	Position Paper: Update on the EFSA NanoGuidance – Francesco Cubadda (ISS, Roma) - Application of nanotechnologies in the agri-food sector: assessment of risks to human health
15:50	Coffee break
16:00 18:00	Companies meet with young researchers Short presentations and face to face meetings Jeol (Italia) SpA, Gabriele Bulla – Living in the future: Innovation of electron microscopy Tec Star Srl, Alberto Borghi – Innovation by nanoparticles Assing SpA, Stefano Chiesa – The research partner NANO SENSOR SYSTEMS Srl, Giorgio Sberveglieri - Metal Oxide Nanowires gas sensors for food quality control EVOpdI Srl, Enrico Luciano Appiani – Our evolution towards catalysis

Saturday, 14 December	
Closing Ceremony <i>Chairs Nelson Marmioli (CINSA, Italy), Lanfranco Masotti (Consorzio Italbiotec, Italy) and Filippo Maurizio Acciarri (Univ. Milano Bicocca)</i>	
9:00	Reporting on sessions from the Scientific Committee
10:30	Coffee break
11:00	Presentation from organizers Best poster and best oral presentations - Special Elsevier AWARDS Conclusion -Where we go from here, <i>Nelson Marmioli (CINSA)</i> Conclusion – <i>Nelson Marmioli, Lanfranco Masotti, Filippo Maurizio Acciarri</i>

Oral Communications

From Science to Technology

Leo Miglio

University of Milano Bicocca, Department of Materials Science

Nanotechnology has a longer history than what is usually supposed it to have. The bio-inspired concept of encoding big data in a tiny space (as related to cracking of the DNA code in 1953) was firstly envisioned in a top-down perspective by Richard Feynman, the Nobel Prize physicist, in the famous CalTech conference of December 1959 “There’s plenty of room at the bottom”. Just sixty years ago. Actually, the very first nanostructured material was obtained a dozen years later by Leo Esaki, the Nobel Prize winner in 1973, who invented the semiconductor multiple quantum-well... and the word “Nano-Technology”. This nanostructure readily entered the industrial production for semiconductor lasers and accompanied the development of the CD players, not limited to this application. The microelectronic industry supported the race towards top-down nanotechnology, accomplishing the requirements of Moore’s law in ICs, independently and previously of the nano-science boom. Nowadays, many self-assembled semiconductor nanostructures are currently studied and implemented for microelectronic, optoelectronic and photovoltaic applications: quantum dots, nanowires, very recently fins and vertical nanomembranes. Still, the challenge for industrial applications are always the same: uniformity in size and shape, ordering in arrays and crystal quality with respect to defects and compositional intermixing. I will discuss these issues, with some examples, and set the point of the complex interplay of thermodynamic and kinetic driving forces in the epitaxial deposition of three-dimensional, faceted nanostructures.

Sustainable innovation of microbiome applications in the food system

Anne Pihlanto^{1*}, Søren J Sørensen², Annamaria Bevivino³, Henk Bolhuis⁴, Minna Kahala¹,
Vesa Joutsjoki¹, Anne-Maria Pajari⁵, Ine van der Fels-Klerx⁶, Jane Maher⁷

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The threat of food insecurity is a critical global challenge, which is compounded by climate change and population growth. Forward-thinking solutions are needed to meet this challenge and recent research has shown the potential of microbiomes to positively impact food production, food and nutrition security and ultimately influence human health. Microbiomes are the community of micro-organisms (bacteria, fungi, protozoa and viruses) living in a certain habitat, such as soil, sea, human or animal body. Microbiomes are known to regulate the productivity and health of major food sources across land and sea. However, we lack a deep understanding of the microbiomes associated with our food systems.

The general objective of “sustainable innovation of microbiome applications in the food system” (SIMBA) is to get a better understanding of microbiomes’ structure and function, related to marine and terrestrial food chains and to verify the sustainability of microbial innovations of the food system as a whole. Our research will result in increased food production and enhanced food quality and safety. Altogether 22 research institutes and industrial partners all over Europe participate in SIMBA. During the four years (2018-2022) of project implementation interdisciplinary research will be performed but also commercial microbial applications will be piloted.

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No. 818431 (SIMBA). This output reflects only the author’s views.

Design of microbial consortia with plant growth-promoting activity for sustainable crop production

Andrea Brunori¹, Marina Caldara², Silvia Tabacchioni¹, Daniel Neuhoff³, Giusto Giovannetti⁴, Stefania Passato⁵, Alessia Fiore¹, Antonella Del Fiore¹, Cristina Cantale¹, Jonas Hett³, Caterina Giovannetti⁴, Patrizia Ambrosino⁵, Chiara Nobili¹, Ombretta Presenti¹, Sarah Frusciante¹, Soren Sørensen⁶, Joseph Nesme⁶, Franziska Klincke⁶, Alexander Sczyrba⁷, Andreas Schlüter⁷, Elena Maestri², Nelson Marmioli², Anne Philanto⁸, Annamaria Bevivino^{1,*}

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Plant Growth-Promoting Microbes (PGPMs) are a potential alternative to chemical fertilizers and pesticides. They are increasingly considered to be an important strategy for sustainable agriculture intensification. PGPMs can improve crop productivity and nutritional quality, as well as resistance to plant pathogens and plant tolerance to abiotic stresses. Most approaches for plant growth promotion imply the use of a single bacterial species as biofertilizer while only few consider a consortium of selected microorganisms. In order to exploit the full agronomic potential of PGPMs for sustainable crop production by optimising the efficacy and reproducibility of field applications, firstly we identified the most promising PGPMs to be applied as bioinoculants on wheat, maize, potato and tomato plants in Italy and Germany. Following a comprehensive literature survey, 46 PGPMs were considered, together with modes of application. Results obtained from the *in vitro* compatibility performed among the 25 available PGPMs enabled two main microbial consortia to be identified, both composed of PGPMs with different functions (i.e., nitrogen fixation, P-solubilisation, biocontrol, amylolytic activity, auxin or auxin-like compounds production), with or without arbuscular mycorrhizal fungi (AMF). As carriers, biochar obtained from wood, methyl cellulose and microbial stabilization following the SME industrial process procedure were considered for the delivery of microbial inoculants in greenhouse experiments. *In vitro* compatibility tests of microbial consortia and bioactive compounds are ongoing as well as greenhouse experiments for testing the effect of microbial consortia on seed vigour, plant growth and microbial activity.

Supported by funding from the EU Horizon 2020 research and innovation programme under grant agreement No. 818431 (SIMBA).

Microbial processing for nutritional enhancement of plant based products

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The importance of cereals and legumes in diets is widely recognized and consumers are looking for ways to balance their diet with plant-based options. However, the presence of antinutritional factors, in particular, in legumes and cereals reduces their nutritional value by decreasing the bioavailability of proteins, minerals and vitamins.

In SIMBA project, the objective of food processing is to find and select bacterial strains for fermentation processes to upgrade the nutritional value and safety of the selected legumes and cereals. Lactic acid bacteria (LAB) have an important role by contributing to the safety, flavour, texture, nutritional value and overall quality of products in food fermentations. LAB fermentation of legumes and cereals has been shown to reduce the level of several antinutrients, like condensed tannins, phytic acid, vicines, galacto-oligosaccharides and, amylase and protease inhibitors. LAB may also bring health promoting features through vitamin synthesis, probiotic effect, and production of bioactive peptides.

Many of the described features are strain specific, therefore both the genome based screening of process strains and literature survey are used for selection of strains for the fermentation processes. Novel techniques, such as high-throughput DNA sequencing technologies and studies on microbiomes has led to deeper understanding on microbial abundances and interactions, as well as influences of the microbial community on metabolite production. As a result of this action in the SIMBA project, a validated production process with application of specific starter strains will be developed and upscaled to a pilot or industrial scale. The main and final goal is a protein-rich food product with improved nutritional value, digestibility, micronutrient bioavailability and food safety for human consumption.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 818431 (SIMBA). This output reflects only the author's views.

Sustainable foods and human gut microbiota

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Our research is an integral part of the SIMBA (sustainable innovation of microbiome applications in the food system) project. Our work package addresses how a sustainable diet or a side stream -derived food produced utilising microbes shapes the human gut microbiota and thereby human health. The specific objectives for our work are

- To determine and model the composition and activity of human gut microbiota in relation to markers of gut and metabolic health by utilizing samples and data from an earlier intervention study with healthy volunteers on a sustainable diet where part of animal protein was replaced with plant-based protein sources.
- To assess the usefulness of using microbes to produce health-promoting food products from side streams by studying the effects of a fermented rapeseed-seaweed product in human subjects suffering from metabolic syndrome.
- To study effects of polyphenols and bile acids identified in the intervention datasets on selected immune and gut epithelial cells *in vitro*.
- To recognize the most significant diet-microbiota interactions in the intervention datasets and potent bioactives from fermented foods, and test them further using cell cultures and bioinformatics tools.

Preliminary results on the effects of replacing dietary animal proteins with plant-based protein sources on the composition of gut microbiota and gut metabolism are available.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 818431 (SIMBA). This output reflects only the author's views.

Sustainability Assessment and Potential Uptake of Innovations

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Contemporary food systems are the major contributor to biodiversity and soil health loss as well as to health problems connected to malnutrition, such as obesity, non-communicable diseases and micronutrient deficiencies. Moreover, they have other significant negative impacts, such as pollution of underground and superficial water bodies, the abandonment of rural territories and loss of cultural resources, as well as climate change. On the other hand, it has been recognized that food systems could become an important driver for change in achieving the Sustainable Development Goals. In this regard, innovations exploiting the knowledge about terrestrial and soil microbiomes are expected to have a significant role to play, if food value chain actors uptake them at scale. The overarching objective of work package 7 (WP7) of the SIMBA project is to increase the innovation capacity of the food system by stimulating the uptake of microbiome-based innovations by actors in food production and by assessing the expected increase in overall sustainability.

For further in-depth investigation, we selected four archetypal European farming system cases, defined by the arable crop and their representative region of production: the potato value chain in the Netherlands and Germany, the wheat value chain in Northern Italy and Germany, the industrial tomato value chain in Northern Italy, and fish (feed) production in Finland. In each case, the baseline (conventional) scenario will be compared with the innovation scenario, in which microbiome-based applications are used in the production process. The uptake of innovations is investigated from a consumers' and a farmers' perspective. In hypothetical choice experiments, consumers' willingness to pay (WTP) is elicited in innovation scenarios compared to baseline scenarios. Online surveys are conducted in the Netherlands, Italy and Germany and will provide information on the value of different attributes of the products. Likewise, the barriers and drivers that influence the farmers' willingness to apply microbiomes is investigated by means of online surveys. Specifically, we will be looking at dispositional factors such as personality, concerns and farming objectives, social factors and cognitive factors, such as knowledge, perceived control, perceived benefits and perceived risks. To assess the overall contribution to sustainability, including environmental, economic and social dimensions, first, a comparative environmental life cycle assessment (LCA) and social-LCA will be conducted for each case. Second, an integrated framework will be used to combine the LCAs' results with findings from an estimation of the economic impacts in an overarching analysis.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 818431 (SIMBA). This output reflects only the author's views.

Effects of Copper Oxide nanomaterial on plant flowering: a transcriptomic and physiological approach to enable sustainable food production

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Literature on beneficial effects of some engineered nanomaterials (ENMs) on edible plants is increasing, both as fertilizer and disease/pest control agents. However, there are some factors which are still limiting the widespread development and application of ENMs including regulatory differences between EU, USA and Asia, and the underlying potential for unknown environmental effects and health risks. Furthermore, the understanding of the chronic low dose ENMs effects on edible tissues is still very limited.

The present study aims to characterize the physiological and molecular responses in zucchini (*Cucurbita pepo* L.), treated with copper oxide (CuO) NPs, from germination to flowering. The physiological analyses have been accompanied with a complete transcriptomic analysis of the different plant tissues. Data obtained demonstrates that the application of high-throughput transcriptomics, coupled with analytical and physiological data, can bridge the gap between genotypic and phenotypic evidence when investigating plant response to ENMs exposure. At the same time, the data show important potential biomarkers of ENM exposure/effect, which may be useful for future risk assessment for food safety and for environmental health.

Nitrate-doped Biomimetic Calcium Phosphate Nanoparticles as N and P Slow-Release Nanofertilizers via Particle Dissolution

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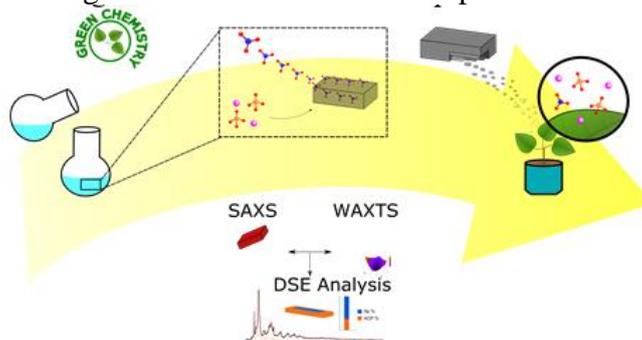
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Global food security is considered as one of the greatest challenges of the 21st century. While crop demand is expected to significantly increase, many of essential resources that support food production are becoming scarce. Therefore, the use of fertilizers to maintain a high agricultural productivity is essential. Unfortunately, conventional fertilizers show a poor efficiency, which has negative environmental and economic implications. Thus, there exists the urgent need of new strategies leading to a more efficient use of agrochemicals. Some recent attempts at addressing agriculture challenges draw on the use of nanotechnology. Several smart nanofertilizers have demonstrated to have a more efficient uptake or/and slow delivery of active ingredients than their bulk counterparts. Based on these considerations, we have designed several engineered calcium orthophosphate nanoparticles doped with nitrate, showing different features in terms of crystallinity, size and composition. The preparation was carried out through a one-pot process, following the green chemistry principles. An exhaustive characterization has been performed by combining Small Angle X-ray Scattering and synchrotron-based Wide Angle X-ray Total Scattering techniques, complemented by Infrared Spectroscopy and Transmission Electron Microscopy. The in-depth characterization, coupled to the stability and nutrient release kinetics, provides information on the structure-properties relation, enabling a slower nitrate release via particle dissolution.



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FePO₄ nanoparticles as a source of nutrients: effects on plant transcriptome and on soil microbial communities and functions

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In the last decade nanotechnology became a substantial part of the technological progress in modern agriculture. Nanomaterials that can provide one or more macro/micro-nutrients to the plant - commonly referred to as nanofertilizers - are employed. In a recent work, Segal et al. (2019) showed that iron phosphate (FePO₄) nanoparticles (NPs) can provide either iron (Fe) or phosphorus (P) to plants in hydroponic systems. The present study aims to highlight the effect of FePO₄ NPs as nanofertilizer on the plant-soil system, considering both the transcriptional responses of plants and the impact of NPs on a plant-soil microcosm. Maize and cucumber seedlings were grown in hydroponic for 24 hours and early transcriptomic responses to FePO₄ NPs exposure in roots were investigated by means of microarray expression analyses. Results showed that several transcripts are modulated depending on the form of FePO₄, indicating that transcriptomic responses are specific for the nano and the non-nano FePO₄. Moreover, two different bare soils were enriched with FePO₄ NPs; soil's enzymatic activity, respiration and DGGE analyses showed that FePO₄ NPs had no effects on soil's microbial community and metabolic functions, nor toxic effects. We observed that FePO₄ NPs can provide similar amounts of available P in the two bare soils with respect to triple superphosphate (TSP) but depending on soil's characteristics. Concerning the plant-soil system, we observed that plants grown with FePO₄ NPs or TSP as source of P showed no significant differences, although P availability in the same bare soil resulted higher for TSP.

Tailoring the chemistry of bioceramic nanoparticles for unconventional applications

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It is nowadays widely demonstrated that nanomaterials, in comparison to their bulk counterparts, possess unique and novel properties that have a huge impact in health, food, environment, and energy sectors. Among them, being similar to the mineral phases of bone and teeth, the generation of synthetic bioceramics based on calcium phosphates (CaP) nanoparticles is of great interest both to prepare more effective and personalized materials usable in the nanomedical field, both to study biominerals mimicking *in vitro* their formation. In addition, CaP nanoparticles have recently attracted great attention as promising materials for applications far from medicine, such as catalysis, water remediation, and agriculture as they represent a more biocompatible and “green” alternative to those currently used. The aim of this talk is to give an overview of the synthetic processes and strategies to produce CaP nanoparticles and how to tailor and characterize their chemical-physical features. Their preparation from biogenic sources using a circular economy approach will be also discussed. The unconventional use of the CaP based nanomaterials in the field of cosmetic, agriculture and environment will be particularly highlighted.

Laser Patterning of Graphene Oxide induce bone regeneration

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Carbon nanomaterials mechanical, electrical, antibacterial and regenerative properties have been largely studied in the last decade. Among these, graphene oxide (GO) and its reduced form rGO have unique biological properties, being able of inducing mesenchymal stromal cells differentiation and promote bone tissue formation with efficacy depending on reductive state of the material. It has indeed been discovered that by controlling the GO oxidative state, the modulation of osteogenic process and bone mineral matrix production by mesenchymal stem cells is controllable. In this study, we laser-printed GO surfaces to obtain both a local photo-thermal GO reduction and the formation of nano-wrinkles along precise patterns. In the first days of culture, cells migrated and accumulated on the reduced and wrinkled surface. When the local density of the stem cells on the reduced stripes was high, cells started to proliferate and occupy also the GO. The designed surfaces morphology guided stem cell orientation and the chemical reduction of material surface accelerated differentiation. Moreover the exposure of GO sheets after laser printing, caused death of Methicillin resistant *Staphylococcus aureus* (MRSA) bacteria seeded on the surface by acting as nanoblade and disrupting bacteria membranes. GO laser printing can become a revolution in present and future trends for patient-tailored scaffolds design for regenerative medicine.

ALD growth of Co thin films on the topological insulator Sb_2Te_3

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The coupling between ferromagnetic thin films (FM) and topological insulators (TI) is attracting huge interest in the context of spintronics. The presence of Dirac-like surface states in the TI, jointly with the large spin-orbit coupling, is expected to favour a super-efficient magnetization manipulation of the FM through an enhanced *spin orbit torque* (SOT). Here, we present the first attempt of employing a pure atomic layer deposition (ALD) process to grow Co thin films on the Sb_2Te_3 TI, grown by Metal Organic Chemical Vapor Deposition (MOCVD). ALD allows a large-scale deposition process with self-limited and conformal growth, although so far scarcely employed for. The ALD of few-tens nm of Co is conducted on top of granular Sb_2Te_3 films and on Pt layers produced by magnetron sputtering. Pt is conventionally used as SOT material, providing an excellent benchmark to evaluate the Sb_2Te_3 properties. The chemical-structural characterization of the Co/ Sb_2Te_3 and Co/Pt heterostructures is performed by X-Ray Diffraction and Reflectivity (XRD/XRR) and Scanning Electron Microscopy (*Figure 1*). XRD showed that Co layers show an hexagonal crystalline structure on Sb_2Te_3 , while they grow in the cubic phase on Pt. Broadband Ferromagnetic Resonance experiments are used to measure the damping and the effective magnetic anisotropy constants of the Co/Pt and the Co/ Sb_2Te_3 heterostructures (*Fig.1(b)*). Complementary information obtained by Vibrating Sample Magnetometry and Brillouin Light Scattering spectroscopy will also be presented. Noteworthy, the combined use of ALD and MOCVD could open interesting possibilities to scale up the manufacture of large-scale devices based on the FM/TI heterostructures.

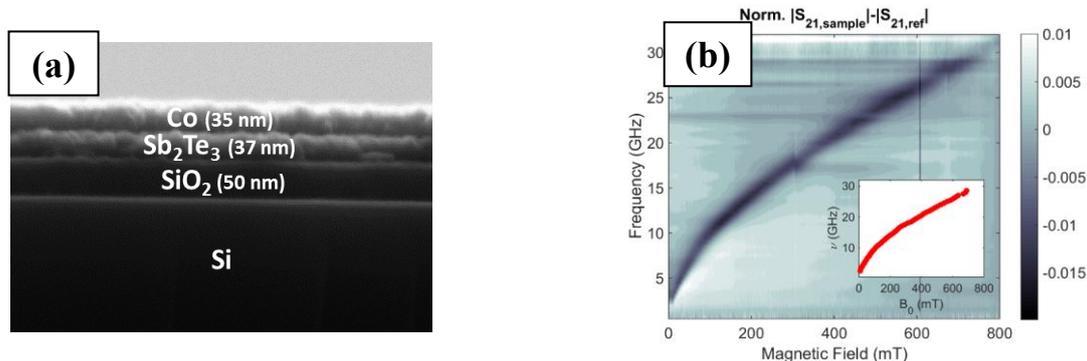


Figure 1: (a) SEM cross-sectional view of a Co/ Sb_2Te_3 heterostructure; (b) Broadband Ferromagnetic Resonance collected data for a Co(50 nm)/ Sb_2Te_3 (37 nm)/ SiO_2 sample. On the x and y axis are shown respectively the quasi-static magnetic field and the microwave frequency applied to the sample. In the inset of (b) the extracted resonant magnetic field values (B_0) versus frequency are reported.

A novel classical approach to optical properties of metal nanoparticles

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Most properties of plasmonic nanostructures follow from the tunability of their optical response as a function of their shape and dimensions; in case interparticle gaps are formed, the so-called “hot-spot” regions occur, in which localized surface plasmons can interact with molecules placed in the junctions, allowing single molecule detection [1-3]. The optical properties of nanostructures are generally treated, independent of the system's size/shape, by resorting to classical approaches [4-6]. However, when the size of the particles or junctions is only a few nanometers or smaller, the quantum nature of electrons emerges, activating quantum tunneling effects across subnanometer interparticle gaps [7-9].

For such a reason, the description of optical properties of subnanometer junctions is particularly challenging. Purely classical approaches fail, because the quantum nature of electrons needs to be considered. In this contribution, we report on a novel classical fully atomistic approach, ω Fluctuating Charges (ω FQ), based on the Drude model for conduction in metals, classical electrostatics and quantum tunneling [10].

We will show that ω FQ is able to reproduce the plasmonic response of both metal nanoparticles and complex metal subnanometer junctions, with quantitative fidelity to full *ab initio* calculations [11-12]. Besides the practical potentialities of our approach for large scale nanoplasmonic simulations, we show that a classical approach, in which the atomistic discretization of matter is properly accounted for, can accurately describe the nanoplasmonics phenomena dominated by quantum effects.

This work has received funding from the European Research Council (ERC) under the European Union’s Horizon 2020 research and innovation programme (grant agreement No. 818064).

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Nanoparticles Localization in Tissues at Sub-Diffraction Level by Infrared Thermal Imaging

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Active photo-thermal imaging over sub-millimeter to centimeter-sized fields of view with tunable resolution in the 10-100 μm range would be a valuable tool for the nondestructive characterization of the morphology and functional state of biological tissues. In nanomedicine and nanotechnological research, for example, high-resolution active thermography would allow mapping the ex-vivo distribution of plasmonic nanoparticles following systemic administration in animal model systems, while simultaneously preserving quantitative information on the laser-induced temperature increments. This is an important step for the subsequent development of photo-thermal therapy protocols to be applied in vivo to the tissue.

We therefore describe and validate here a non-contact photo-thermal super-resolution image acquisition approach. We combine the photo-thermal effect induced by the sample absorption of modulated laser light with the a-posteriori localization of the resulting laser-induced temperature variations. By the surface fit of the isolated temperature peaks imaged by a low-cost thermal camera, light-absorbing and heat-releasing centers get localized and rendered in the final super-resolution image. While best-fit amplitudes color-code for local temperature values, peak coordinates provide morphological information on the sample with a resolution assigned by the $\sim 10\text{-}\mu\text{m}$ excitation laser-spot size.

We initially validate the proposed approach on synthetic ink samples and demonstrate thermal imaging at 60- μm resolution, thereby proving a resolution gain of a factor of 6 and 20 with respect to the 350- μm diffraction-limited prediction and the effective 1200- μm resolution of our thermal camera in conventional operation. We further perform proof-of-principle experiments on complex biological samples, and image explanted murine skin biopsies treated with Prussian blue 30-nm nanocubes. With photo-activated temperature increments as low as 0.1-2 $^{\circ}\text{C}$, we provide temperature-based super-resolution maps of the distribution of the absorbing nanostructures across mm-sized tissue sections.

Telecom InAs QDs grown by Droplet Epitaxy on vicinal GaAs(111)A

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Droplet epitaxy (DE) is very powerful growth technique, performed in Molecular Beam environment (MBE), in order to fabricate quantum dot (QD) structures. In comparison of conventional Stranski-Krastanov growth mode, DE is not a strain-driven technique, thereby, it is possible to use wide range of materials and substrate orientations to obtain QD nanostructures with necessary parameters. Also, DE is a promising method for producing low-density QDs for single and entangled photon emitters. In order to create highly entangled photon pair, it is necessary to eliminate anisotropy-induced fine-structure splitting (FSS). It is possible to realize by symmetric QDs grown on (111) surfaces with natural C_{3v} symmetry. Lattice-matched GaAs/AlGaAs QDs system is well studied and it emits at a wavelength of approximately 700-800 nm. In order to shift wavelength of emission up to telecommunication band (1.31 – 1.55 μm), it become necessary to change heterostructure composition. One possible way is to fabricate InAs QDs on metamorphic InGa(Al)As layer, grown on GaAs substrates.

In this study, we have investigated the fabrication of InAs QDs on InAlAs metamorphic layer grown on vicinal GaAs(111)A substrate with 2° miscut towards $(\bar{1}\bar{1}2)$. We have found conditions to grow flat InAlAs layers (RMS < 0.5 nm). Using DE method, we obtained InAs QDs with a density of about $1 \times 10^8 \text{ cm}^{-2}$. This approach results in QD emission wavelength of about 1.3 μm with a low FSS of exciton-biexciton cascade (< 5 μeV), which is necessary for long-distance quantum key distribution.

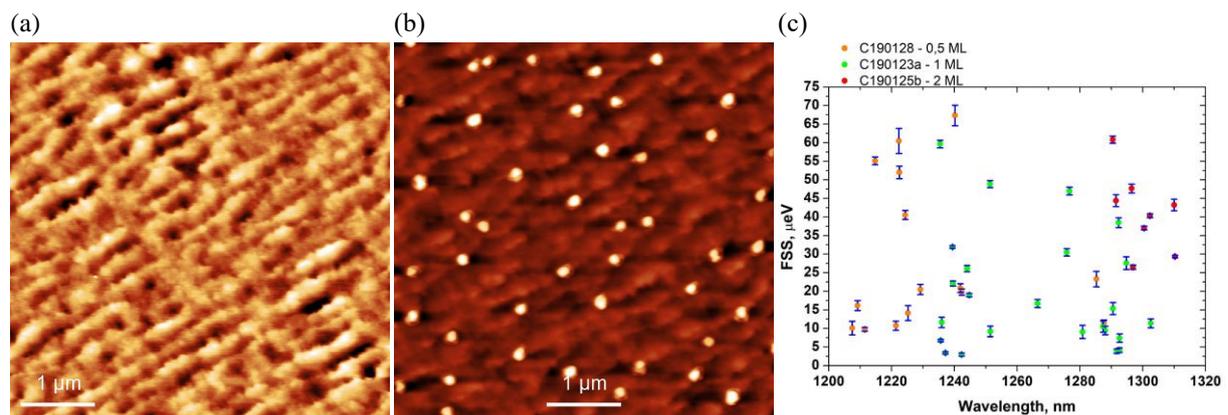


Fig. 1. (a) and (b) AFM images ($5 \times 5 \mu\text{m}$) of InAlAs metamorphic layer and InAs QDs on InAlAs metamorphic layer, grown on vicinal GaAs(111)A with 2° miscut towards $(\bar{1}\bar{1}2)$, respectively. (c) Distribution of emission wavelength and FSS of InAs QDs with different size.

In-flow Synthesis of Multibranched Au/TiO₂ Hybrid Nanosystem: Exploiting the Plasmonic Features for Catalytic Purposes

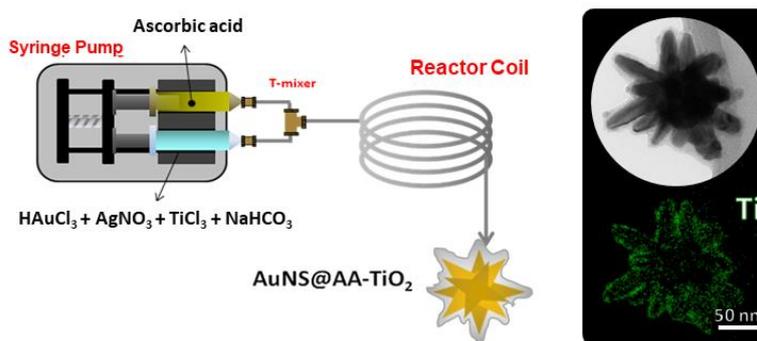
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Plasmonic nanosystems built by metal/semiconductor hybrid nanoparticles had shown promising applications enabling an efficient solar light harvesting and enhancing the photocatalytic activity. Core-shell systems as Au-TiO₂ nanoparticles are ideal candidates due to the dynamic synergy established at the interface able to improve the e⁻/h⁺ pairs separation and stability. Recently, anisotropic AuNPs gain increasing interests thanks to their tunable localized surface plasmon resonance band (LSPR) in the visible range.¹ However, reliable protocols to synthesize anisotropic AuNPs covered with TiO₂ by direct wet chemistry approaches is still challenging.² Herein, we report a novel synthetic protocol for the preparation of star-shaped AuNPs (AuNS) functionalized with nanostructured thin TiO₂ layers, by exploiting a designed bench-top microfluidic reactor.³ This one-pot seedless procedure is based on the accurate mixture of gold and titania precursors that allows the direct and continuous production of AuNS@TiO₂ without adding any stabilizer agent. The hybrid composites exhibit a stable red-shift LSPR band and a good dispersibility in water and alcohols. Au/TiO₂ nanosystems show under simulated solar light a catalytic photoactivity toward the Rhodamine-B degradation. Before the photocatalytic tests, any eventual residual ligand on the NP surface has been cleaned-off by treating NPs with H₂O₂, affording purified hybrid nanosystems highly active and water dispersible.

AuNS@TiO₂ were fully characterized by UV/vis, ICP-OES, HRTEM, STEM, EELS map to disclose the Ti distribution. This innovative procedure is reproducible and scalable, allowing the production of a high amount of shape-controlled AuNS@TiO₂ hybrid nanoparticles, dispersed in solution and easy to concentrate in small volumes.



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Synthesis, characterization and application of low band gap rod-coil block copolymer water-processable nanoparticles, synthesized by surfactant-free miniemulsion approach

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Water-processable nanoparticles (WPNPs) of hydrophobic conjugate polymers is an intriguing technology, which find huge applications in optoelectronics, biology, and medicine. We focused on four amphiphilic low band gap rod-coil block copolymers (BCPs) constituted by a rigid hydrophobic p-type semiconductor polymer, PCPDTBT, and 4-vinylpyridine-based (4VP-based) coil block which replace the surfactant role interacting with aqueous medium.

We prepared stable WPNPs in water through a surfactant-free miniemulsion approach, exploiting the presence of the coil block, composed of 4VP repeating units, in the BPC backbone, stabilizing the nanostructure. Four coil blocks having different molecular structure and length were studied in order to identify the coil influence on the structure and stability of WPNPs. We mixed the BPC with five 4VP repeating units an electron acceptor fullerene derivative ([6,6]-phenyl-C₆₁-butyric acid methyl ester, PC₆₁BM) to gain blend WPNPs (b-WPNPs)

We deeply characterized the obtained suspension using TEM, STEM-EDX, EFTEM, AFM, and DLS in order to elucidate the role of the 4VP-based coil blocks on the WPNP morphology and stability.

In particular, the STEM-EDX maps showed that the rod block, containing sulfur atoms, stays mainly in the inner part of the WPNPs, while the 4VP-based coil on edge. Moreover, the EFTEM images of the b-WPNPs identify the PCBM nano-domains. We tested the obtained B-WPNPs as active layer in organic solar cells made through sustainable processing (PCE 2.5%).

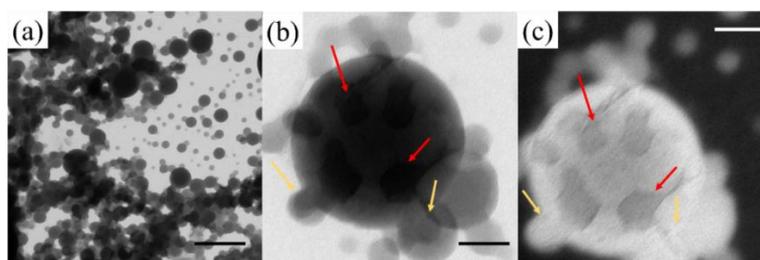


Figure BF-TEM images of the a) BCP5:PC₆₁BM (1:3) blend NPs, b) detail of one blend nanostructure, and c) corresponding EFTEM image. The scale bars are (a) 500 nm and (b,c) 50 nm, respectively. Red and yellow arrows emphasize the differences observed between BF-TEM and EFTEM images.

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Nanotoxicology: focus on the impact of metal and metal oxide nanoparticles

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The increasing production of engineered nanomaterials (ENMs) necessitates that close attention be paid to potential adverse effects on human health and the environment. Metal and metal oxide nanoparticles have been the subject of numerous toxicological investigations in recent years. However, a detailed understanding of the mechanism(s) of toxicity is still lacking. Our laboratory has been engaged in several EU-funded nanosafety projects including FP7-NANOMMUNE, FP7-MARINA, FP7-NANOREG, FP7-SUN, and FP7-NANOSOLUTIONS, and we have screened a large number of ENMs using primary immune-competent cells or cell lines in the frame of these projects. Further studies are under way in H2020-BIORIMA (biomaterial risk management), and in the national MISTRA Environmental Nanosafety consortium. In the present lecture, some lessons learned in these projects will be discussed. Focus will be afforded, in particular, to our recent work on amorphous silica nanoparticles. Detailed physicochemical characterization of the test materials and the need for a common standard for reporting of experimental results must also be considered.

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Towards the Risk Governance of Nanotechnologies: the ISS Multidisciplinary Unit

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European Commission (EC) considers Nanotechnologies as one of the six Key Enabling Technologies (KETs) for society and economy, and EU Member States included them among the priority issues for human health and the environment (Parma Declaration on Environment and Health, WHO 2010). Moreover, it is now recognized, both from regulatory agencies (e.g. OECD, ECHA, EFSA, EMA) and from the international scientific community, that the integration of different experiences and competences is essential to ensure a safe and responsible development of these technologies in the different areas of production and use in order to move towards a specific governance framework for nanotechnologies. In the perspective of the need of a co-ordinated approach to address nanomaterial (NM) safety the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) has recently established a Multidisciplinary Unit on Nanomaterials and Nanotechnologies. Goal of this unit is the identification of the possible risks and benefits for human health and environment deriving from the use of NMs and the adoption of the strategies to mitigate any risks. The Unit includes one Department and 5 National Centers of ISS. Its multidisciplinary character allows to aggregate different competences in order to achieve the common objective: the consolidation and the increase of knowledge on NMs, both through the pursuance of ongoing activities and through the finalization of new project proposals. The multidisciplinary nature is also essential to face in a coordinated way to specific requests of the National Health Service, in line with the institutional role of ISS.

Immune characterization of graphene-based materials for the design of new tools in biomedicine

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The possible immune modulation by graphene-based materials (GBMs) is a fundamental aspect for any translational application into clinical practice. We previously demonstrated that the different physicochemical properties dramatically modulate the impact on human immune cells [1-4]. Here we exploited innovative approaches, such as single-cell mass cytometry to evaluate the impact of a large set with different lateral size dimensions of graphene oxide (GO) and amino-functionalized GOs (unpublished data). The presence of amino groups on GO surface increased its immune compatibility and was also able to induce a specific M1 like activation on monocytes and the secretion of interleukin-4 and Granzyme-B from B cells, skewing a cytotoxic-like response. Moreover, we combined graphene with inorganic quantum dots containing indium therefore enabling for the first time the detection of graphene on single cell mass cytometry and on a large variety of primary immune cells. Our results demonstrated that monocytes and, unexpectedly, B cells, showed a superior ability to internalize the GO compared to the other immune cell subpopulations. Finally, the immune modulation of a specific GO was exploited in combination with the osteoinductive capacity of calcium phosphate to design a new nanomaterial (magoCAP); we obtained an increased bone regeneration *in vitro* and *in vivo* via magoCAP treatment) [5]. Our results demonstrate that specific design and functionalization of GBMs offer new strategies for the modulation of immune cell functionality. The immune cell functionality governs every aspect of our health, therefore the GBM-based immune modulation paves the way for of future biomedical application design.

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Exploiting blood nanoparticles for augmented pathogenesis identification

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Blood is a very complex biofluid, composed of water, cells, soluble factors and nanoparticles (NPs). Blood NPs, from the long known lipoproteins to the recent discovered extracellular vesicles (EVs) represent a breakthrough in medicine since they participate in the regulation of both physiological and pathological processes. Current knowledge on blood NP is fragmented, sectorial, focused on a specific biological and/or medical aspect of a given NP subtype, often due to technical difficulties in studying these structures.

Our lab started to study blood NPs with an innovative multidisciplinary approach combining classical biological and biochemical analyses with determination of biophysical and colloidal properties.

Our studies revealed that blood NPs are a powerful tool to understand the pathogenic mechanisms underlying hematological disorders like Multiple Myeloma (MM) and Monoclonal Gammopathy of Undetermined Significance (MGUS) and genetic disorders like the Down Syndrome (DS). EV number density, specific protein composition, internalization rate and pro-inflammatory processes activation help differentiation of serum derived MM EVs from the asymptomatic premalignant stage MGUS. All these elements could be used as precocious biomarkers and a complementary approach for the differential diagnosis. On the other hand, specific microRNAs associated to plasma NPs can give new insight on the biomolecules involved in the DS clinical features, hidden and/or not accessible to standard and classical analysis.

Graphene Quantum Dots for the Treatment of Glioblastoma Multiforme

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Glioblastoma is one of the most aggressive human brain cancers with very short survival times. Due to the low and strictly selective permeability of the blood-brain barrier (BBB), such cerebral tumors are inaccessible to traditional therapies. Therefore, the development of a strategy to cross the BBB and target malignant cells has a crucial importance to make chemotherapeutic treatments effective. Some nanoparticles have shown the capability of passing through the BBB, both in in vitro and in vivo models. This feature is tightly dependent on their size and surface chemistry. In the last years, graphene quantum dots (GQDs), nanoparticles of dimensions below 20 nm, have shown the capability of crossing several biological barriers, as well as good biocompatibility. Recent studies have also highlighted that different functional groups on GQDs surface can affect their cellular uptake, intracellular distribution and relative biological responses. In this study we show how three different surface chemistries of GQDs regulate biocompatibility in two cellular populations: U87 glioblastoma cells and neurons. We investigated the effect of a combined therapy of GQDs with doxorubicin (DOX). We pointed out a synergic effect of the co-administration of DOX and GQDs, finely modulated by their surface chemistry. We demonstrated that the synergic effect is mediated by a modification of membrane permeability due to surface chemistry of GQDs. Taken together, those findings strongly highlight that GQDs play two key roles in the treatment of glioblastoma: they can cross biological barriers and destabilize cell membrane, thus increasing the efficacy of chemotherapeutic drugs.

Selective Modulation Of A1 Astrocytes By Drug-Loaded Nano-Structured Gels In Spinal Cord Injury

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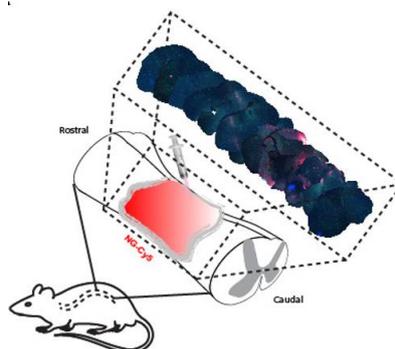
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Spinal cord injury (SCI) is a frequent disabling injury of the spine that leads to cell degeneration, involving neurons, astrocytes and oligodendrocytes¹. Secondary processes (e.g. inflammation, apoptosis and oxidative stress) cause additional loss of neurons and glial cells (secondary injury). After an acute damage, the reactive pro-inflammatory response of the astrocytes, with the subsequent formation of scar tissue and the inhibition of axonal regrowth, is pivotal. Astrocytes with A1 phenotype exert indeed neurotoxic effects, upregulating genes associated with the synapse and neuronal degeneration, suggesting that A1 has harmful pro-inflammatory action². Various approaches have been employed to counteract this detrimental progression of the secondary injury³. For this purpose, a large number of NP systems have been tested, but none are selective for pro-inflammatory astrocytes⁴. Therefore, the challenge is to formulate a targeted, effective therapy with neuronal protective effects, reducing the side effects.

In this study we have developed a novel delivery tool, a nanogel-based nanovector able to be selectively internalized in activated astrocytes. When loaded with Rolipram, an anti-inflammatory drug, this nanovector allows a selective and controlled release in the spinal cord, reversing the toxic effect of A1 astrocytes on motor neurons *in vitro*. When tested acutely in a SCI mouse model it improves motor performances, reducing the astrogliosis and preserving neuronal cells.



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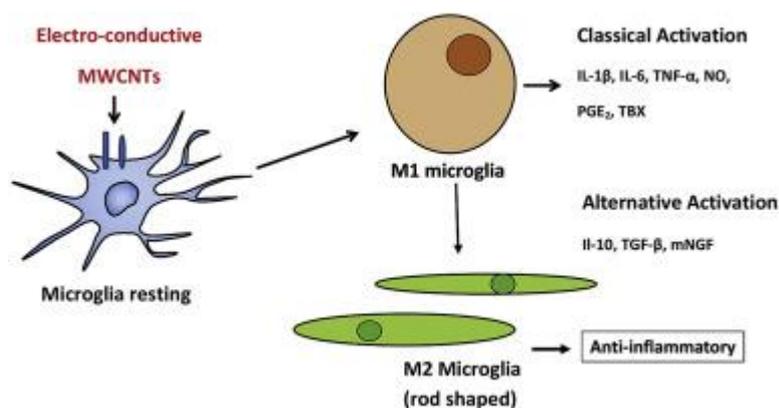
Neuroprotective effect of Metallic Multi Walled Carbon Nanotubes

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CNTs have been recently investigated for applications in nervous tissue engineering. Microglia are considered as the brain's resident immune cells that are activated in response to inflammatory stimulations and neurological injuries. Microglia “M1” phenotype is involved in the regulation of brain development by enforcing, through the production of pro-inflammatory molecules, the elimination of damaged neural cells. Microglia “M2” phenotype enhances neuronal survival through the release of trophic and antiinflammatory factors and cytokines and is involved in neurogenesis. We demonstrated that electro-conductive MWCNTs (a-MWCNTs) increase significantly the release of proinflammatory factors (NO, iNOS) and cytokines (IL-1b,TNF-a) by microglia after 24 h exposure. This activity decreased at 48 h while a shift to an increase of antiinflammatory cytokines (IL-10 and TGF-b1) and neurotrophic factors (mNGF) occurred. In a-MWCNT exposed cells, the “M2” phenotype was particularly expressed at 48 h, and most of them were found to be bipolar/rod-shaped with a neuro-protective role. The transition to “M2” phenotype microglia and the release of antiinflammatory cytokines and neurotrophic factors seem extremely important to support the capacity of these CNTs to modulate microglia behavior. Our data suggest that the electrical properties of CNTs could be exploited to stimulate microglia anti-inflammatory potential



Mucoadhesive Polymeric Inserts containing Cyclosporine-A loaded Nanomicelles for the Treatment of Dry Eye Syndrome: Technological and Biopharmaceutical Characterization

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Purpose of this work was the preparation of mucoadhesive inserts containing cyclosporine-A loaded nanomicelles to obtain both the increase of drug solubility and the CyA ocular bioavailability by improving the precorneal residence time.

First, drug-loaded nanomicelles were prepared by mixing two non-ionic surfactants (Vitamin E-TPGS and Octoxynol-40) with cyclosporine-A (0.1%w/v) in water and characterized by size, drug entrapment and loading. Then, the nanomicelles were incorporated into five inserts obtained by solvent casting of different mucoadhesive polymers dispersions. The inserts were characterized in terms of weight, thickness, drug content, wettability, mechanical properties (folding endurance, tensile strength) and dissolution test. In addition, the morphology of the insert was verified by SEM. The nanomicelles formation after insert solubilization in water was verified. Uniform distribution of CyA-nanomicelles in the inserts was confirmed by confocal analysis after loading the nanomicelles with a fluorescent probe. Finally, in vivo animal ocular tolerability and pharmacokinetic in tear fluid was evaluated.

The CyA-loaded nanomicelles, introduced in round shaped inserts, had ~10 nm size with a good entrapment and loading. Inserts showed suitable features and drug content for ocular application. Only one of tested inserts had a good surface and a slow drug release. Moreover, this system showed better PK parameters than marketed Ikervis as well as a good tolerability. In conclusion, the combination of nanomicelles and mucoadhesive polymeric solid inserts can improve drug bioavailability as a result of the increased resident time in the precorneal area with a good ocular tolerability compared to marketed Ikervis.

***In vitro* toxicity of antibacterial metal oxide nanoparticles: effects on 2D and 3D skin and lung models**

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The massive use of nanomaterials (NMs) in many fields of application poses a growing concern about human safety, especially when skin contact and/or inhalation occur. In this work, the toxicity of different antibacterial metal oxide nanoparticles (MeO-NPs) used for the coating of biomedical textiles, was assessed using different 2D and 3D *in vitro* models of the skin and the lung. NPs suspensions were characterized by TEM and DLS, while NPs-coated textiles were subjected to extraction procedure in artificial sweat (AS, pH 4.7 and 6.5). The release of NPs and/or ions from the textiles after extraction was evaluated through ICP-OES.

For skin contact exposure, Epiderm™ 3D *in vitro* models (MatTek) were used according to the Skin Corrosion OECD TG 431 protocol and to the Skin Irritation test (ISO/TC 194/WG 8 for Medical Devices). Balb/3T3 fibroblasts were used as 2D model of wounded skin. For inhalation exposure, A549 lung cell monocultures and an *in vitro* model of the lung barrier cultivated at the Air Liquid Interface (ALI) were used. Data evidenced that, even if MeO-NPs have great potential in the biomedical field, their ability to induce toxic responses may vary depending on the different properties of the NPs and the characteristics of the different models used. In conclusion, in order to fulfil the knowledge gaps and ensure a safe and sustainable design of NMs, it would be pivotal to include exposure and hazard assessment in the experimental researches.

Integrated and distributed sensors for the IOT

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“In a future of connected devices, embedded sensors are the interface between computers and the physical world”. The huge innovations related to the connection of distributed devices in a localized network, up to the IOT approach, are based on new classes of sensors, that are not only miniaturized, but effectively functional parts of the products. The goal is not to attach standard sensors to functional materials, but to exploit all the strategic properties of the material structure, to obtain innovative and unprecedented features. Examples of this approach are presented in different class of materials. Direct functionalization of textile fibers, allows to obtain wearable organic electrochemical transistor, that are able to monitor human sweat, to control dehydration and to measure biological parameters of interest¹. The textile biosensors, being part of cloth fibers, are able to naturally absorb the sweat, simplifying the sample collection. Another example, is the integration of piezoelectric nanoxiedes on carbon fibers², to obtain pressure sensors, embedded in composites materials. The complete integration of the piezo active materials, allows to maintain the specific strength and lightness in the composites. Moreover, the functionalization of porous polymeric sponges, with conductive polymer, produce an active material, in which the compression is proportional to resistance modifications. With this embedded functionalization, soft pressure sensors, have been realized and integrated in foot insole and in artificial soft skin for robots. Finally, the ability to control surface properties, by fine tailoring surface hydrophobic properties, in electrochemical sensing devices, has improved selectivity, due to diffusion solute properties. The improved devices have been used to determine successfully the presence of cancer cells, respect to healthy samples, in secretome of primary cultures³.

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Nanomechanical resonators from suspended DNA fibers for structural analysis

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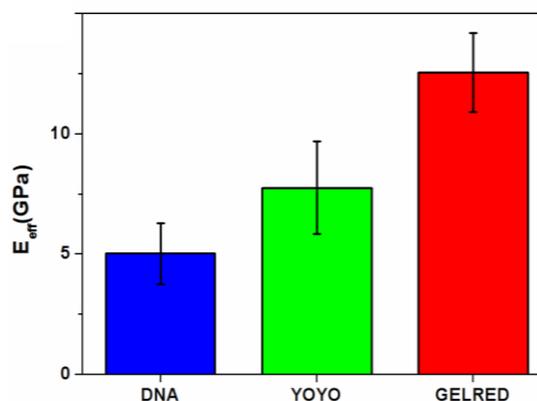
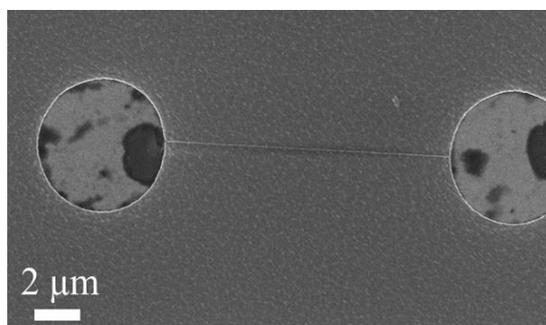
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The understanding of how aromatic molecules interact with DNA is of fundamental importance in several biological processes. While base pairing is conserved, DNA/ligand complexes are affected by altered mechanical properties, due to the local modification in size, density and rigidity. Such variations significantly perturb the DNA biological function, disturbing fundamental cellular processes such as reparation, replication or transcription.

We here propose to investigate such biomolecular mechanism thanks to a radically new approach based on nanomechanics of suspended DNA resonators. The isolation of oscillating DNA molecules is technically very challenging, but recently the team conceived a super-hydrophobic technique to suspend DNA bundles of pristine and intercalated strands over circular pillars [1]. Thanks to a laser Doppler vibrometer with sub-picometer resolution [2], the mechanical resonances of such DNA nanobridges will be assessed. The obtained results will allow a deep understanding of how intercalation affects mass, density, stiffness and dissipation of DNA/ligand structures, thus paving the way to nanomechanical fundamental studies of DNA interaction also with other ligands, such as proteins and heavy metal ions.



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The Role of Advanced X-ray Scattering Techniques on Nanomaterials Characterization: A case study on CdSe-based Colloidal Quantum Dots

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In the last decades, the scientific and technological interest in nanostructured light-emitting materials has enormously increased.[1,2] II-VI engineered semiconducting nanomaterials offer a precious contribution in the field of technology and applications thanks to their tunable optical properties and extraordinary stability over time even in the presence of external stimuli.[3,4] This aspect makes this class of materials ideal for applications in devices such as displays and photovoltaics. The surface engineering of the II-VI semiconductors has allowed the increasing of the photoluminescence quantum yield (PLQY) by covering the emitting core with one or more layers of an isostructural compound, removing surface trap states that affect the emission properties of the nude core.[5] For this reason, the in-depth characterization of the crystalline shell is fundamental in correlating the increase of the PLQY with the structural and microstructural changes induced by the passivating shell. Nevertheless, despite the functional characterization has reached its maturity for these materials, their structural and microstructural characterization is still a weak point and suitable forefront characterization approaches need to be developed. Aiming at filling this gap, our recent work has shown that it is possible to exploit a combination of X-ray scattering techniques, in the small and wide angle regime, jointly to advanced modelling techniques based on the Debye Scattering Equation (DSE).[6] This approach has been developed and applied to colloidal CdSe [7] and core-shell CdSe@CdS quantum dots in order to correlate structural defectiveness with the functional properties of these materials. The models presented can be easily extended for characterizing II-VI homo- and hetero-structure nanomaterials.

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Aromatic Imides Functionalized Cellulose Nanosponges for Naked-Eye Heterogeneous Sensing of Fluoride

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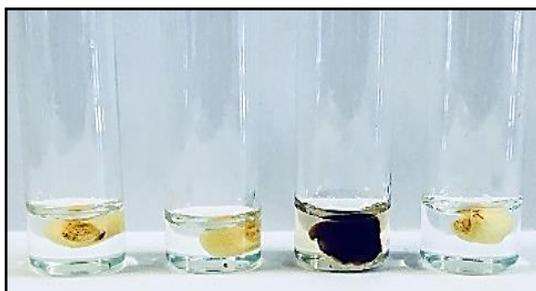
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Interest towards nanocellulose as building blocks for the design of innovative materials is continuously increasing as a result of its several valuable properties. Nanocellulose can be easily obtained through several mechanical or chemical approaches, acting on the hierarchical structure of cellulose, one of the most abundant renewable biopolymers in nature (Thomas *et al.*, Chem. Rev. 2018).

An easy and scalable protocol for the production of cellulose nanofibers (CNF) consists in TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl radical)-mediated NaClO/NaBr oxidation of C6 alcoholic groups of glucopyranosic units to the corresponding carboxylic acids (Pierre *et al.*, Carbohydr. Polym. 2017). This approach gives TEMPO-oxidized cellulose nanofibers (TOCNF) characterized by micrometric length and nanometric diameter.

Herein we present a series of novel solid-state sensor materials based on branched polyethyleneimine functionalized with aromatic mono- and bisimides sensor units supported onto TOCNF by thermal copolymerization (Melone *et al.*, ChemPlusChem 2015). These materials are capable to selectively recognize fluoride anion by the “naked-eye” when dipped into DMSO solution containing the target analyte at a concentration of at least 0.05 M. Interference from other interfering anionic substrates, such as acetate and phosphate, is negligible and they can be easily reused for several times without apparently losing their sensing ability (Riva *et al.*, ChemPlusChem 2019).



Sponge-like materials able to selectively recognize fluoride anions in solution by a colour change visible to the *naked-eye*

Tailoring optical properties and stimulated emission in nanostructured polythiophene

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Polythiophenes are semiconducting polymers widely employed in organic electronics; however, in optics and photonics, their use is limited by high photo-induced absorption due to the presence of interchain polaron pairs, preventing the establishment of net optical gain. In our work¹, we study the photophysical properties of poly 3-hexylthiophene (P3HT) with different degrees of supramolecular ordering. In particular we focus on spin-coated thin films and templated nanowires (NWs) fabricated with a soft nanolithographic approach², characterized by a high degree of supramolecular ordering and a defined spatial organization. We performed transient absorption (TA) measurements, to compare optical properties of P3HT NWs and spin-coated disordered films. In the NWs samples, experimental results evidence the presence of a partially-polarized stimulated emission band, in contrast with the photo-induced absorption band observed in spin-coated films and assigned to polaron pairs³. TA results, combined with theoretical modelling, assign the origin of the primary photoexcitations, with singlet excitons. In spin-coated films, there is a different localization of electrons and holes over individual polymeric chains, which might favor intra- and interchain separation of the carriers and subsequent formation of polaron pairs. In the ordered configuration, this effect is suppressed and we have an optical gain. Thus supramolecular ordering of the polymer chains is a powerful strategy to directly control optical properties of P3HT. Moreover, this work opens new perspectives for the use of polythiophene nanostructures in organic optical amplifiers and active photonic devices.

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Perspectives on Nanostructured Architectures for Biosensing Applications and New Analytical Tools: Toward Precision Medicine

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There are two key aspects that have to be taken into account when dealing with precision medicine, particularly in oncology field: early diagnosis and therapeutic treatment, two sides of the same coin strictly related to each other. In fact, early diagnosis is crucial to assess whether an individual is (already) or can be affected by a cancer form or not, and, in case the response is positive, what is the correct therapeutic regimen he or she has to undergo to. Both these aspects require (i) a reliable and minimally invasive procedure capable of detecting circulating cancer biomarkers, and (ii) a fast (possibly in real-time) therapeutic drug monitoring (TDM) to prevent severe toxic side effects, which ultimately might cause death. More reliable, fast and sensitive analytical tools are thus highly sought. In this presentation I will show recent advances concerning the development of new nanostructures architectures, based on novel and promising bio-receptors, and newly developed analytical tools, based on electrochemical and optical analytical techniques, which can be conveniently coupled to improve both diagnostics and TDM while providing important physico-chemical information about the experimental conditions under investigation. In particular, coupling electrogenerated chemiluminescence (ECL) and surface plasmon resonance (SPR) can be highly beneficial to develop new sensing platform with unprecedented capabilities.

Magnetic nanoconjugated glycopeptides as novel tools for bacterial infection site targeting

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Nanoconjugated antibiotics are considered as next generation drugs as they possess remarkable potential to overcome multidrug resistance in pathogenic bacteria. Iron oxide nanoparticles (IONPs) have been extensively used in biomedical applications thanks to their biocompatibility and magnetic properties. More recently, IONPs have been also investigated as potential nanocarriers for antibiotics to be magnetically directed to or recovered from infection sites.

Our goal is conjugating to IONPs the glycopeptides teicoplanin and vancomycin - ‘last-resort’ antibiotics used for treating severe infections by multiresistant Gram-positive pathogens^[1]- by surface functionalization with (3-aminopropyl)triethoxysilane (APTES)^[2]. Classical microbiological methods, fluorescence and electron microscopy were used to evaluate antimicrobial activity and surface interaction of naked, functionalized, and glycopeptide-conjugated NPs in comparison to non-conjugated teicoplanin and vancomycin. As bacterial models, differently resistant strains of Gram-positive bacteria (*Staphylococcus* spp., *Enterococcus faecalis*, and *Bacillus subtilis*) were used. Results indicated that glycopeptide antibiotic conjugation might confer high and prolonged antimicrobial activity to IONPs towards these Gram-positives. Sensitivity of bacteria to NPs varied according to the bacterial surface, being species-specific. Additionally, conjugation of teicoplanin and vancomycin improved the cytocompatibility of IONPs towards two human cell lines and, finally, NP-TEICO inhibited the formation of *S. aureus* biofilm, conserving the activity of non-conjugated teicoplanin versus planktonic cells and improving it towards adherent cells.

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Intercalation of Bioactive Molecules into Nanosized ZnAl Hydrotalcites for Combined Chemo and Photo Cancer Treatment

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Hydrotalcites-like compounds (HTlc) also known as anionic clays or layered double hydroxides, represent a class of lamellar solids with net positive charge balanced by exchangeable interlayer anions¹. HTlc are excellent materials for designing drug delivery systems due to their biocompatibility, ability to intercalate different anionic species, pH-dependent stability and low toxicity². The present study focuses on the preparation of HTlc intercalating separately two different molecules: the anticancer drug norcantharidin (NCTD), which is known for inducing cell cycle arrest at G2/M phase and the tetra-sulfonated aluminum phthalocyanine (AlPcS₄), a photosensitizer used in photodynamic therapy³. The obtained hybrid ZnAl HTlc were characterized in terms of X-Ray powder diffraction pattern, thermogravimetric analysis, SEM microscopy, drug release profile, *in vitro* cytotoxicity and ability to produce ROS and ¹O₂ upon light irradiation. Our results clearly indicate that the two selected compounds are efficiently intercalated within HTlc layers. Moreover, *in vitro* preliminary studies on a panel of cancer cells lines indicated a greater cytotoxicity of the two drugs once loaded on HTlc either when administrated singularly or in combination. In addition, the analysis of the synergistic effect of the two formulations was evaluated by determining their combination index, which showed a greater cytotoxicity when using as a 1:2 ratio of AlPcS₄@HTlc and NCTD@HTlc, respectively.

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Critical issues in the clinical translation of nanobiotechnology research and future directions of nanomedicine

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In the last two decades, nanotechnology has offered a variety of innovative solutions that allow clinicians of the 21st century to design innovative therapeutic and diagnostic strategies by taking advantage of nanomaterials with unique optical, electronic, thermal and magnetic properties, as well as improved solubility and biocompatibility.

The recent advances achieved by researchers in the development of targeted nanocarriers together with a faster data collection deriving from the study of their communication with the biological environment has generated optimistic expectations for the rapid translation of this basic research into the clinical practice with immediate benefits for patients. However, despite the considerable success achieved, nanotechnology has not yet met its potential as a sustainable technology. To make a step forward in this direction, it is crucial that the engineered nanomaterials that gain entry into the marketplace are both effective and safe. Indeed, the uncertainty surrounding the toxicity of nanomaterials deserves thorough investigation of the consequences of their use on human health and of the environmental impact. Discussion on nanosafety is often related to toxicology, ecotoxicology, exposure assessment, risk assessment and the need for standardization. The latter is particularly relevant for regulatory purposes, as rapid material categorization according to human health and environmental risk may allow for expedited review of newly proposed nanomaterials and nanodrugs. As a matter of fact, only a few nanodrugs have been approved for specific disease treatments so far, which has raised some criticisms on the real effectiveness of nanomedicine compared to the large amount of resources dedicated to the research in nanobiotechnology.

This talk will present the main challenges that the scientific community and industry should face to bring the new discoveries to an established practice that would allow the regulatory bodies to accelerate the process toward clinical translation of nanodrugs. First of all, a well standardized toolkit for the categorization of all newly developed nanomaterials – including appropriate material characterization, biological characterization and details of experimental protocols – should be defined before they can be approved for use in humans. Furthermore, standardized assays for the assessment of short-term and long-term toxicity of nanoparticles will also need to be defined in 2D/3D cell cultures and animal models before approval for clinical trials.

Finally, based on the available information, an overview of the principles in developing safe-by-design nanomaterials for biomedical applications is proposed. These principles may also serve as a basis for the categorization of broader more effective safe-by-design strategies.

Toxicity of Metal-Based Engineered Nanoparticles in Crops and Their Impact on Global Food Security and Safety

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Widespread use of metal-based nanoparticles (NPs) such as oxides of silver (Ag), titanium (Ti), zinc (Zn), and rare earth elements (REE) including cerium (Ce) and Indium (In) in the environment has raised some serious concerns about their adverse effects on the agriculture and environmental and human health. In this study, the effects of these NPs exposure on several plants including Arabidopsis, rice and soybean were investigated at the physiological, biochemical, and molecular levels. Our results demonstrate that most of these NPs induce severe oxidative stress and causes significant membrane damage. The levels of malondialdehyde (MDA), an important indicator for membrane damage, and antioxidant enzymes such as SOD, CAT, APX, PPO and POD that scavenge ROS under stress conditions were also significantly higher compared the untreated plants. We also evaluated the effect of Ag NPs exposure on soybean growth, yield, and nutrient displacement. Our results showed that even a low level of Ag NPs exposure severely affect the N fixation abilities of soybean as it inhibit the nodule formation and reduce overall plant growth. Total N contents were significantly decreased in nodules, roots and shoots. Exposure of plants to Ag and other metal oxides NPs also inhibited Fe and other nutrient element uptake in plants. Speciation analysis of Ag using XAFS is soil and soybean tissues indicated the transformation of Ag NPs to Ag ions, which were conjugated to GSH. Further, the expression of genes involved in sulfur assimilations and GSH biosynthesis pathway was significantly higher compared to non-treated plants. These results indicated that GSH could be a key redox molecule in the cells to counteract the toxicity of Ag NP and other metal oxides and manipulation of genes related to GSH homeostasis can reduce the nanotoxicity in crop plants. These studies are helpful in understanding the fate, transport, and toxicity of NPs in the agricultural crops and to develop strategies for minimizing their impact on food crops.

Amorphous silica nanoparticles interfere with LPS-dependent metabolic changes in human macrophages

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We have previously demonstrated that precipitated (NM-200) and pyrogenic (NM-203) Amorphous Silica (AS) nanoparticles (NP) elicit inflammatory activation of murine macrophage cells, with more pronounced effects observed with NM-203. In this study, we compare the biological activity of the same ASNP in human macrophage-like THP-1 cells assessing cell viability, autophagy, mTOR signaling, ER-stress, Glutamine Synthetase (GS) expression, NFκB-dependent inflammatory response and caspase-1 activation. Low, non-toxic doses of both ASNP do not interfere with the LPS-dependent activation of NFκB, the transcription of its target genes *PTGS2* and *IL1B*, or mTOR activation. Conversely, they cause the blockage of autophagy, as indicated by the increase of p62 abundance, a phenomenon that was more evident in NM-203 treated cells. NM-203 inhibited more effectively also two LPS-dependent effects, the activation of ER-stress and the increase of GS expression. The latter phenomenon is possibly functional to the recovery of the intracellular [Gln], which decreases during the first phases of LPS-dependent activation. Moreover, silica NP inhibit caspase-1 cleavage, hindering the relative LPS-dependent stimulation of IL-1β secretion. The effects of ASNP on autophagy, as well as on GS expression and Gln metabolism, were reproduced also in primary macrophages derived from human peripheral blood. Thus, low doses of amorphous silica NP modulate several important metabolic pathways in human macrophages altering their response to LPS challenging. As far as autophagy, ER-stress and GS expression are concerned, NM-203 are more effective than NM-200, confirming the high biological reactivity of pyrogenic amorphous silica NP.

Use of chitosan nanoparticle to vehicle dsRNAs against tomato spotted wilt virus in plants

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Double stranded (ds) RNA-based vaccination is a promising technique to immunize plants against viral infection via application of exogenous dsRNAs. However, the rapid degradation of the dsRNAs is a limiting factor and dictates to explore suitable delivery agents such as nanovectors, aiming to stabilize them. We investigated the use of chitosan nanoparticles as carriers of dsRNAs against tomato spotted wilt virus (family *Bunyaviridae*) infection, aiming to get a slow and controlled release of this active principle. Chitosan was the carrier selected as it is largely available, cheap, and fully biocompatible and biodegradable. Nanoprecipitation was evaluated to produce nanoparticles using the vortex mixer or the confined impinging jets reactor. The latter was shown to provide better results as the size of the nanoparticles is more reproducible and the scale-up to industrial-scale units is easier. Chitosan nanoparticles obtained by this way had a mean size ranging from 200 to 300 nm, depending on the operating conditions, being stable for several weeks. A dsRNAs loading higher than 80% was achieved; when the release from nanoparticles was evaluated *in vitro* through dialysis, we observed that about 95% was released in the first 48 hours, indicating that this system may achieve the desired targets *in vivo*. With the final goal of evaluating the efficacy of dsRNA-loaded nanoparticles *in vivo*, current studies are focused on the optimization of nanoparticle synthesis process and features in order to further increase their loading ability and decrease the release rate of the active molecules.

Eco-design of nanostructured cellulose sponges for sea-water decontamination from heavy metal ions

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The growing human activity on the sea coasts is more and more associated to a progressively increasing of seawater pollution. Ship operational discharges, local accidents and illegal activities often lead to detect ppm concentrations of heavy metal ions in marine waters. The use of engineered nanomaterials (ENMs) is emerging as a valuable alternative for environmental remediation. However, the concerns related to ENMs potential ecotoxicity still limit their use in real scenarios. The correct choice of the starting material and of the synthetic protocol could provide new safe-by-design solutions for this purpose. Following this approach, we report the eco-design strategy used for the development of eco-friendly cellulose-based nanostructured sponges (CNS) which resulted to be effective sorbent units for heavy metals removal from seawater. The materials were obtained following a two-step protocol, consisting first in the production of TEMPO-oxidized cellulose nanofibers, followed by their cross-linking in the presence of branched polyethyleneimine. CNSs obtained exhibit high performances in removing a wide range of heavy metal ions (Zn(II), Cd(II), Cr(III), Hg(III), Ni(II), and Cu(II)) from sea water. Environmental safety of materials (ecosafety) was investigated by using a standardized ecotoxicity bioassay as algal growth inhibition test (OECD 201) coupled with an *in vivo* exposure study using a filter-feeder marine bivalve species in which immune cells viability and genotoxicity were investigated. The results in terms of eco-safety evaluation led to the optimization of the material synthetic strategy (eco-design) and allow to combine the best decontamination efficiency with no risk for aquatic biota.

Direct effects of diesel exhaust particles on different cell lines as well as on *in vivo* rat heart: Euro III vs. Euro IV engines

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Air pollution is identified as an important matter of cardiovascular disease in urban communities and exhaust nanoparticles (NPs) from Diesel engines (DEP) may contribute greatly to the health effects of Particulate Matter (PM) in urban environments. Prompt exposure to PM has been associated to a plethora of adverse cardiovascular events. Moreover, diesel soot emitted by modern engines exerts cytotoxicity. A detailed evaluation of cardiac electrophysiological effect and related mechanisms is missing and is the main goal of the present work. We administered DEP-NPs, collected from Euro III (DEPe3) and Euro IV (DEPe4) engines (that includes Diesel particulate filter), on pulmonary and cardiac cell lines *in vitro* and, intra-tracheally, on *in vivo* rats. No macroscopic differences were observed between DEPe3 and DEPe4, while SEM analysis revealed that DEPe4 contained more NPs compared to the DEPe3. Moreover, different metal content was observed in DEPe3 compared to DEPe4 soot. The clonogenic test showed a rapid internalization of DEPe4 compared to DEPe3 in HL1 cardiac cell line and an inhibition of proliferation activity in cultured pulmonary A549 compared to HL1 cells, treated with both DEP-NPs. Oxidative stress also provoked lipid peroxidation, highlighted by significant increases in TBARS in both cell lines after DEPe3 and DEPe4 treatments. *In vivo* evaluation demonstrated that DEPe4 treatment affect significantly cardiac electrophysiological compared to DEPe3 treatment. We demonstrated that Diesel soot, emitted by modern engines, jeopardizes cardiovascular electrophysiology rather than old engines probably due to i) rapid internalization ii) small aerodynamic diameter of NPs and iii) different metal content.

Chemo-enzymatic oxidation of plant galactomannans with laccase/TEMPO for production of renewable biomaterials, also as delivery systems

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Sustainable development requires renewable resources that should offer several advantages such as readily and next to unlimited availability, plus minimal environmental impact. In recent years, polysaccharides of natural origins, mostly obtained from plants, have attracted considerable attention as potential replacements for traditional synthetic polymers, made from fossil-derived monomers. Polysaccharides, either in their natural or chemically/biochemically modified forms, have a broad spectrum of industrial applications, including in pharmaceutical, food and livestock feed, cosmetics and packaging industries. In our work, recent results of enzyme oxidation of galactomannans (GM) from leguminous plants (fenugreek, sesbania and guar), with laccase, instead of galactose oxidase, are presented. We discuss the simple and efficient fungal laccase/TEMPO oxidative reaction of galactomannans from a few leguminous plants endosperms, which causes an over 15-fold viscosity increase of GM solutions and a transition of the gels from a viscous to an elastic form, presumably by formation of emiacetalic bonds and internal crosslinking of the polymers. Lyophilization of the hydrogels generate stable aerogels, capable of uptaking and retaining active principles from aqueous solvents. After re-lyophilization, the “loaded” aerogels can release the actives and inhibit the growth of bacterial cultures. To test this potential application, the following molecules were uploaded, retained and released from re-lyophilized GM aerogels against Gram positive or negative bacteria: the antimicrobial peptide nisin; the enzyme lysozyme; the antibiotic polymyxin B; the mixture of the industrial biocides 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one. The results obtained open the way to the generation of new functionalized biomaterials with tailored properties as delivery systems of actives.

Reference Materials for Environmental Nanoplastic Pollution

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Plastic pollution is a global challenge that strongly impacts the environment and human health. More recently, minute fragments at the micro and nano-scale originating from the breakdown process of bigger pieces have become of increasing concern, driving the research efforts toward the understanding of sources, distribution, fate and impact of these particles. However, micro and nanoplastics have the main limit to be small in size, negatively affecting the development of adequate methods for qualitative and quantitative studies. In this framework, there is a strong need to create good reference materials at the laboratory scale, mimicking as closely as possible the real particles. Environmental sub-micrometer particles are far from being modelled by ideal particles commercially available, synthesized with the desired size, shape, surface, and composition. For these particles there are no reason for a selection in size, they could have asymmetrical shape and heterogeneous surfaces.

In this contribution, we will present a methodological pathway to study micro and nanoplastics through the preparation of more realistic reference materials. Starting from commonly used disposable plastic items, we use different techniques to fragment or degrade macro pieces in a controlled way, such as mechanical disruption or photodegradation. We include methods for preconcentration and separation of the plastic particles into specific size fractions. Finally, our approach combines consolidated techniques in the field of nanomaterials analysis, such as imaging techniques, size distribution and physical-chemical characterization techniques, as vibrational spectroscopy, to fingerprint nanoplastics through ad hoc analytical nanochemistry.

Maintenance and expression of organelle information in plants exposed to engineered nanomaterials

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One of the challenges potentially limiting the continued widespread commercial development and application of engineered nanomaterials (ENMs) is the still perceived lack of knowledge on their potential environmental effects. Although evidence has been accumulating on the biological effects of ENMs at the level of cells, tissues, and organisms, wide differences in experimental design make their use difficult for a systemic analysis. More importantly, environmental risk assessment procedures are not sufficiently harmonized. Mitochondria and chloroplast in higher eukaryotes are not only the energy power plant of the cells but have an important regulatory and developmental role. Experimental data have shown that mitochondria and chloroplasts are between the primary targets of metal-based ENMs. To provide a unifying picture of the molecular mechanisms of nanomaterial action, the aim of this work is to examine critically the instances of mitochondria and chloroplasts involvement in ENMs response, in terms of preservation of organelles vs DNA duplication. This work highlights critical parameters to consider when designing sustainable ENMs and suggests to use it as an endpoints that can be sought when assessing the impact of ENMs exposure on environmental and human health.

Regulatory aspects of nanomaterials issue: towards safe, sustainable and responsible innovation

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It has been 10 years since the European Parliament has called European Commission to establish a comprehensive science-based definition of nanomaterials in Community legislation as part of nano-specific amendments to relevant horizontal and sectoral legislation. Since then many regulatory activities were initiated and successfully accomplished and various legislations were amended to explicitly address nanomaterials ensuring their safe use. Much effort was put in investigations of the adequacy of the chemical risk assessment framework for nanomaterials. While great progresses have been made the detailed methodology and concrete conclusions on safety of nanomaterials and products containing them are still not fully developed leaving regulators and producers trapped in the matrix of complexity and uncertainty.

The fast pace at which nanotechnology is currently evolving and new more advanced, smart nanomaterials emerging may further challenge the regulators' response time for providing tools and amending legislations if needed as the standard information requirements may not always be sufficient to demonstrate the safe use of these new materials.

What are the possible ways to minimize this information gap? How can the industry reduce uncertainties and risks to humans and the environment from the upstream, early phases of the innovation process? How can regulators improve the anticipation in order that they can facilitate the development of adaptable regulation that can keep up with the pace of knowledge generation and innovation? Can the Safe Innovation Approach with its pillars: "Safe-by-design" and "Regulatory Preparedness" be seen as a tool enabling regulatory authorities, innovators and industry to ensure the safety of innovative nanomaterials more efficiently?

Development of a rapid and low-cost microfluidic process enabling efficacious and specific CD44 targeted delivery by using HA-based nanoparticles

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Tumor targetability and site-specific drug release are still critical key factors for cancer therapy and selective drug delivery nanoparticles (NPs) can represent the most challenging opportunity. Coating NPs with hyaluronic acid (HA) can endow nanocarriers with active targeting towards cancer cells marked by CD44 membrane receptor. To date, HA-based nanocarriers are mainly prepared with troublesome, time-consuming techniques.

This research seeks to develop a one-step microfluidic technique for the synthesis of HA-coated NPs, exploiting the ionotropic gelation between HA and chitosan (CS), in order to improve quality, reproducibility and possible scale-up of NPs preparation.

HA/CS NPs have been loaded with Everolimus (EVE), now approved for the treatment of advanced cancers, mostly of them characterized by CD44-overexpressing feature.

A staggered herringbone micromixer (SHM) was used to set-up HA/CS NPs preparation. HA and CS ionic complexation was confirmed by FT-IR analysis. NPs were characterized by TEM and DLS. Placebo NPs biocompatibility was evaluated by MTT assay. Fluorescence HA/CS NPs were prepared using rhodamine-CS conjugate. Cell uptake and trafficking of fluorescent NPs were examined by confocal microscopy in mesenchymal stem cell (MCs) from human bone marrow, characterized as CD44 overexpressing cells by immunocytochemistry assay. EVE cell proliferation inhibition was evaluated by bromodeoxyuridine assay.

SHM-assisted ionotropic gelation method revealed to be a robust, reproducible technique to precisely induce electrostatic interaction between CS and HA for producing NPs with tailor made sizes effectively loading EVE in a high-throughput manner. The actively targeted HA/CS NPs developed herein allows for CD44-overexpressing cells selective uptake.

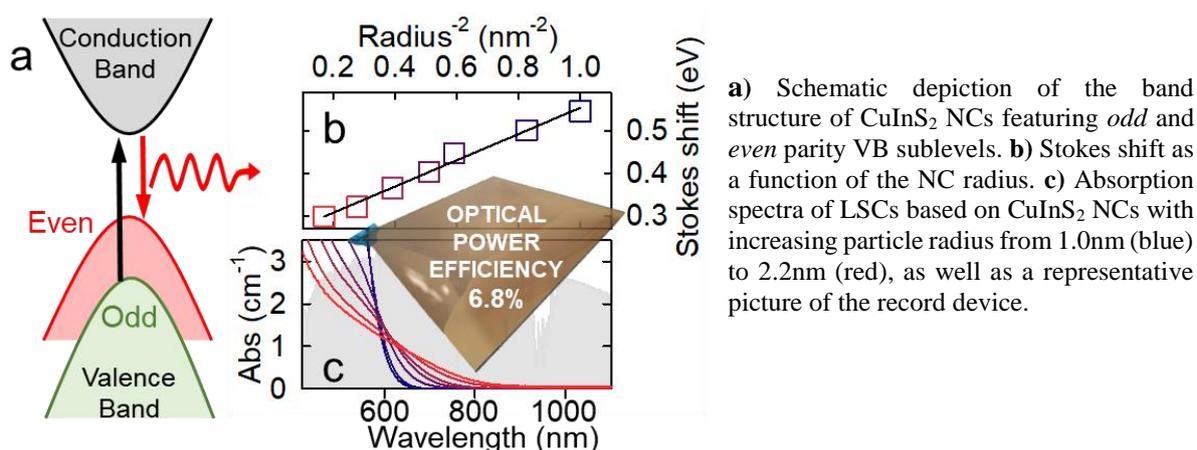
Evidence for the Band-Edge Exciton of CuInS₂ Nanocrystals Enables Record Efficient Large-Area Luminescent Solar Concentrators

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Ternary I-III-VI₂ nanocrystals (NCs), such as CuInS₂, are receiving attention as heavy-metals-free materials for solar cells, luminescent solar concentrators (LSCs), LEDs and bio-imaging. The origin of the optical properties of CuInS₂ NCs are however not fully understood. A recent theoretical model suggests that their characteristic Stokes-shifted and long-lived luminescence arises from the structure of the valence band (VB) and predicts distinctive optical behaviours in defect-free NCs: the quadratic dependence of the radiative decay rate and the Stokes shift on the NC radius. If this origin is confirmed, this will have crucial implications for LSCs devices as the large solar spectral coverage ensured by low bandgap (large size) NCs will come with a cost in terms of increased reabsorption of the guided near-IR luminescence. Here, this hypothesis is tested by studying stoichiometric CuInS₂ NCs of varying sizes, revealing for the first time the spectroscopic signatures predicted for the free band-edge exciton, thus supporting the VB-structure model. At very low temperatures, the NCs also show dark-state emission that had so far never been reported in I-III-VI₂ NCs, likely originating from enhanced electron-hole spin interaction. The impact of the observed optical behaviours on LSCs is evaluated by Monte Carlo ray-tracing simulations. Finally, based on such theoretical insights, optical-grade large-area (30×30 cm²) LSCs with optical power efficiency as high as 6.8% are fabricated, corresponding to the highest value reported to date for large-area devices.



Nanoplatelets Light Emitting Diodes with tunable cathode and anode interfaces properties

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Nanoplatelets (NPLs) are promising candidates for the up-coming new generation light emitting diodes (LEDs) thanks, not only to their efficient, easy-tunable and narrow-band luminescence but also to their ultrahigh color purity. Moreover, NPLs are obtained by a facile synthesis and can be processed from solution. These characteristics allow low-cost and easy deposition techniques, fundamental for opto-electronic devices.

To maximize the efficiency of the NPLs-based LEDs, we are able not only to engineer the level alignment with the metallic cathode by using suitable electron-injection conjugated polymer, but also, by introducing the right functional polar groups, we are able to form strong dipole interactions between interlayer and cathode. The both actions control the injection of the electrons in the device and allow the use of less reactive metallic cathodes.

In parallel, we also worked on the hole injection layer to maximize the shelf-lifetime of the device upon exposure in air by replacing the hygroscopic and acid poly (3, 4-ethylenedioxythiophene) : poly (styrene-sulfonate) (PEDOT:PSS) with an optimized hybrid ink containing an hole-conductive conjugated polymer and two dimensional nanometric-sized Molybdenum Sulfide (MoS₂) sheets.

The combination of these modifications on the device architecture, permitted us to reach a record efficiency (8.39%) for NPLs-based LEDs, an extremely low turn-on voltage (~2 V) and an increasing of the lifetime of the device, maintaining over than 50% of the initial efficiency, up to 100 days for an unsealed device exposed in air.

Thanks to our study, we can firmly confirm that NPLs are excellent candidates for efficient, long-term stable and color-saturated LEDs for display technology.

Nanosized and single site zinc-based activators for reducing ZnO in rubber vulcanization process

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Sulfur vulcanization is a consolidated process for industrially preparing rubber nanocomposites (NCs), based on the formation of sulphide bridges between polymer chains. Reaction rate and efficiency are increased thanks to accelerators (sulphenamides), activators (metal oxides) and co-activators (fatty acids). ZnO is the primary industrial activator, because zinc ions are able to influence both reaction kinetic and mechanistic aspects. Nevertheless, drawbacks are the low dispersion of ZnO, the low affinity with rubber, the use of high ZnO amount (3-5 parts per hundred rubber) and environmental issues, due to zinc release during tyres lifecycle.

In this scenario, aim of the work is the development of innovative zinc-based activators for rubber vulcanization process, to reduce the amount of microcrystalline ZnO, keeping a high vulcanization efficiency. Thus, the introduction of nanosized ZnO particles and single zinc sites anchored onto surface silica particles has been proposed (ZnO/SiO₂ and Zn/SiO₂, respectively), to increase zinc distribution, while increasing its availability and reactivity.

The syntheses of the materials were studied and their properties deeply investigated, through structural, morphological and surface analyses. The experimental characterization of ZnO/SiO₂ suggested the formation of amorphous nanosized ZnO particles covalently bonded to silica; besides, isolated zinc centres coordinated to two amine groups were detected in Zn/SiO₂ activator.

Both ZnO/SiO₂ and Zn/SiO₂ were tested as activators in rubber NCs and compared to microcrystalline ZnO; higher vulcanization efficiencies and improved mechanical properties were achieved, with increased cross-linking densities, using half of the conventional amount of ZnO.

Interfacial properties in composite nano-systems for energy harvesting

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Composite nanostructures can be efficiently applied for Sunlight detection and conversion and, more in general, for energy harvesting and generation of solar fuels. In most of the applied systems, like photodetectors, excitonic solar cells and (photo)-electrochemical cells to produce solar fuels, nanomaterials can play a critical role in boosting photoconversion efficiency by ameliorating the processes of charge photogeneration, exciton dissociation and charge transport. Critical role in such processes is played by the structure and quality of the interface, which needs to be properly assembled to obtain the desired functionality. Several strategies can be pursued to maximize energy harvesting and storage, including broadening of light absorbance to reduce solar light losses, fastening exciton dissociation and charge injection from the photoactive medium to the charge transporting materials, reducing charge recombination during charge transport and collection at the electrodes. In this lecture, a few examples of application of nanocomposites will be thoroughly discussed, including all-oxide coaxial p-n junction nanowire photodetectors and solar cells, core-shell quantum dot fluorophores for high-efficiency luminescent solar concentrators, composite sulfides for hydrogen generation, and oriented carbon nanotube forest dispersed in polymer matrix as efficient low-temperature thermoelectric composite. Emphasis will be given to the role of interface engineering in improving the efficiency of energy conversion in different systems, spanning from electric power generation from Sunlight, to chemical fuel production, to conversion of heat lost through thermoelectric materials.

Validation of a novel argininocalix[4]arene macrocycle as transfection agent for miRNA-mimicking and anti-miRNA molecules

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MicroRNAs (miRNAs) are short non coding RNA molecules able to regulate gene expression repressing translation or inducing degradation of the target transcripts. Altered expression of miRNAs are involved in the pathogenesis of several human diseases, making them key molecular target for the development of innovative therapeutic strategies (i.e. miRNA targeting or miRNA mimicking). The efficient and non-toxic delivery of premiRNA (to obtain miRNA replacement) and anti-miRNA molecules (for miRNA targeting strategies) might be of great interest. An argininocalix[4]arene nanosystem¹ (argininocalix[4]arene **1**) was tested for its ability to deliver miRNA, premiRNA and anti-miRNA molecules to target cell preserving their biological activity. This study points out that: (a) the toxicity of argininocalix[4]arene **1** is low and it can be proposed for long-term treatment of target cells, being this feature a pre-requisite for the development of therapeutic protocols; (b) the delivery of premiRNA and anti-miRNA molecules is efficient, being higher when compared with reference gold-standards currently available; (c) the biological activity of the delivered premiRNA and anti-miRNA molecules is maintained. The argininocalix[4]arene **1** was employed in miRNA therapeutic approaches performed on three well-described experimental model systems, (a) the induction of apoptosis mediated by anti-miR-221 in glioma U251 cells², (b) the induction of apoptosis induced by premiR-124 in U251 cells³ and (c) the inhibition of pro-inflammatory cytokines: IL-8 and IL-6 in cystic fibrosis IB3-1 cells⁴. Our results demonstrate that argininocalix[4]arene **1** should be considered a useful delivery system for efficient, low cytotoxic, transfection of premiRNA and anti-miRNA molecules, preserving their biological activity.

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From food industry by-product to a novel UV filters production for sunscreen applications

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Fisheries produces huge quantities of by-products rich in calcium phosphate, in particular made up non-edible portions of fish (thorns and scales). Only almost 41 wt % of the catch is consumed, while the remaining part is largely disposed of as waste with a negative impact for the environment and the economy of the companies. Furthermore, the world fish production is increasing and will reach 200 million tons by 2020. This means that the wastes will reach 120 million tons by 2020. For these reasons, it is necessary to find a redesigned model that permits to reuse by-product for different applications in a circular economy view. The aim of the work consist in a thermal treatment on fisheries by-products, in particular fish bones, in order to obtain a biocompatible powder capable of filtering UV radiation. This material may replace common nano-sized UV filters (ZnO or TiO₂) present in sunscreen lotion that are harmful for costumer or environment. Indeed, when common UV filters are exposed to UV radiation, they could generate photocatalytic degradation processes that lead to mutagenic molecules production unsafe to the costumer and toxic to sea creatures. The obtained material was characterized by FT-IR, DLS, FEG-SEM and UV spectrometry, and compared with the common UV filters.

Elucidating crop plant response to engineered nanomaterials using metabolomics and proteomics

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Engineered nanomaterials (ENMs) have the potential to improve crop yields, providing protection against pests, improving nutrient delivery and enhancing particular characteristics of food products. In order to gain a higher resolution view of the molecular mechanisms that are influenced by ENMs, we have employed metabolomics and proteomics on a number of crop plants exposed to various ENMs. Proteomic characterization of ENM-treated plants can identify the proteins and associated interactions that are differentially regulated in response to ENM exposure, providing a link between altered gene expression and metabolic processes⁴. In addition, analysis of plant metabolites provides snapshots of the biochemical processes modulated by ENMs exposure. An integrated approach efficiently provides a holistic overview of the signaling processes and biological pathways regulated by ENMs. There are a number of challenges in using these advanced omics approaches, but our studies serve to establish the major metabolic pathways that are perturbed by these interactions. These include glutathione metabolism, tricarboxylic acid cycle, glycolysis, fatty acid oxidation and biosynthesis of phenylpropanoid and amino acids. This information can then be used to select and design better ENMs to achieve the desired outcomes while minimizing toxicity.

Nanotechnology in agriculture: Balancing applications and implications

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Achieving and sustaining global food security will become increasingly difficult as a changing climate increases crop loss due to greater pest and pathogen activity. Nano-enabled agrichemical delivery platforms offer a unique potential to manage pathogens and increase productivity with reduced negative environmental consequences. Work at the Connecticut Agricultural Experiment Station is focused on the sustainable use of nanoscale micronutrients to suppress crop diseases through modulation of plant nutrition. Much of the focus has been on using micronutrient nanofertilizers to manage soil-borne fungal pathogens such as *Fusarium* and *Verticillium*, with the intent of uncovering mechanisms of action and of developing applications that can readily be applied to the field. In one series of experiments, the potential of several Cu nanomaterials to enhance the nutrition and growth of tomato, eggplant, watermelon, and soybean upon fungal infection was evaluated. The particles were foliarly applied once (100-500 mg/L; 1-2 mL dose) to seedlings prior to 30-40 days of growth in the greenhouse or full life cycle in field studies. In control plants, fungal infection reduced plant growth by up to 65% across all species. Amendment with nanoscale Cu significantly reduced disease presence. For example, with tomato in a greenhouse study, disease was reduced by an average of 31-40%, resulting in significantly greater plant biomass. Similar findings were reported for field studies with tomato, eggplant and watermelon. In tomato, the time-dependent expression of genes integral to plant defense (PTI5, PPO, PRP1A1) was shown to be uniquely modulated by nanoscale Cu amendment. In fact, $\text{Cu}_3(\text{PO}_4)_2$ nanosheets increased the expression of all 3 genes within the first 7 days of pathogen exposure, which was prior to any phenotypic evidence of disease. Importantly, these nanoscale Cu-induced changes in expression correlated well with positive changes in disease suppression and plant growth. Similar findings were reported for soybean in another greenhouse study and also for other materials, such as nanoscale mesoporous silica. Importantly, any application of nanotechnology in agriculture must include a thorough understanding of potential implications of this strategy. For example, work from our group has shown that certain nanoscale materials may offer some benefit to the plant but may also cause negative changes in the microbial community in the plant rhizosphere. Collectively, these results highlight the importance of supplemental nutrition in crop disease response and demonstrate the potential of nanoscale platforms to more effectively and sustainably deliver critical micronutrients at early stages of plant development.

A 3D bioprinted model for *in vitro* nanotoxicological investigation: preliminary studies.

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The increasing demand for new and different *in vitro* models, representing better the biological systems capable to cover the gap between conventional cell culture and animal models, contributes in employing (bio)additive manufacturing process to obtain 3D organ models *in-vitro*. Here we present, via a customized 3D bioprinter, the possibility to perform, *in vitro*, 3D models for nanotoxicological studies. The scaffold, containing either Calu-3 or L929 cells, was gently extruded printing a layer-upon-layer following specific and desired spatial geometries. Although it was observed minimal cell death throughout 21 days, cell number was stationary in the scaffold until day 14th where both cell lines duplicated twice in 21 days. This was accompanied by a significant reduction of oxidative stress level overtime, measured by lipid peroxidation assay (TBARS) together with a minimal operational intervention (no cell passage has been performed). Either forty-nanometers polystyrene fluorescent or twenty-nanometer silver nanoparticles have been added on top of the cell-laden scaffolds followed by toxicological and optical assays. We observed, via multiphoton microscopy, that viable cells embedded into the 3D scaffolds were capable to entrap nanoparticles that diffused in all printed layers after 24 hours. Moreover, it has been observed a significant increment of Calu-3 viability comparing 3D and 2D culture exposed to the same rising concentrations of silver nanoparticles. In conclusion, we demonstrated that cell behave different once cultured in 3D and the possibility to perform prolonged nanotoxicological investigations into 3D bioprinted cell-laden scaffolds.

Nanoparticles based on chitosan-derivatives as delivery systems for natural cherry extract polyphenols

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Polyphenols are biologically active substances contained in plants derivatives, which present antioxidant and anti-inflammatory properties. However, they have a limit represented by a low oral bioavailability, since their chemical structures are easily degraded in the gastrointestinal (GI) tract, before to reach the blood. Previous studies reported nanoparticles (NPs) aptitude for internalization by endothelial cells as well as improvement of entrapped polyphenols antioxidant activity. This study aims at evaluating the efficacy of chitosan derivatives (Ch-der) NPs as delivery systems for the oral administration of natural polyphenols-rich cherry extract (CE) from *Prunus avium* L. CE-loaded NPs based on two different chitosan (Ch) derivatives, i.e., quaternary ammonium-Ch (QA-Ch) and S-protected QA-Ch (QA-Ch-S-pro) conjugates, were prepared by ionotropic gelation with hyaluronan and characterized for size (300 nm range) and CE entrapment efficiency, which was around 80%. Human umbilical vein endothelial cells (HUVECs) viability after treatment with the NPs formulations, and consequent oxidative or inflammatory stress induction, was evaluated by WST-1 assay. Moreover, the CE-loaded NPs intestinal permeability was studied in a triple cell co-culture model (Caco-2/HT29-MTX/Raji B). Finally, the NPs uptake by HUVECs has been seen through confocal laser scanning microscopy. The results show that QA-Ch and QA-Ch-S-pro NPs enhance CE anti-inflammatory and antioxidant activity, respectively. Thanks to their mucoadhesive properties and positive surface charge, both NPs types can efficiently interact with cells and promote CE polyphenols intestinal absorption, by protecting them from GI degradation. Therefore, Ch-der-based nanosystems can represent a useful solution for the oral delivery of CE polyphenols.

Superclusters of neuronal cells on zinc oxide nanowires surfaces

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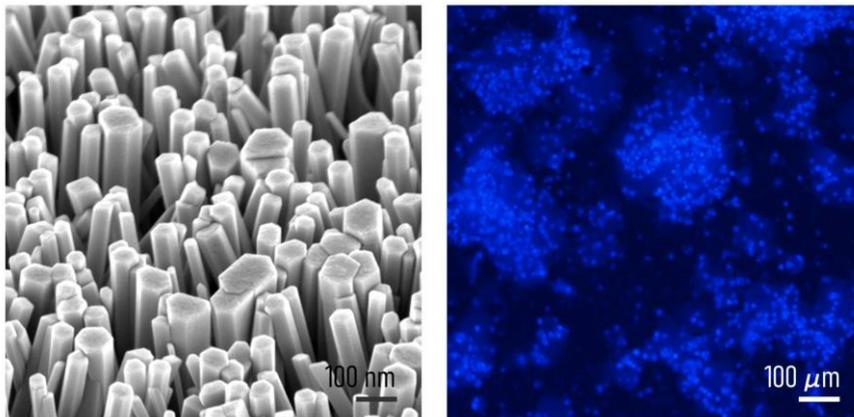
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Neuronal cells are the smallest building blocks of the central and peripheral nervous systems. Information in neural networks and cell-substrate interactions have been heretofore studied separately. Understanding whether surface nano-topography can direct nerve cells assembly into computational efficient networks may provide new tools and criteria for tissue engineering and regenerative medicine. Here, we used zinc oxide nanowires with controlled topography as substrates for neuronal cell growth. We observed that neuronal cells form networks that exhibit a high sensitivity to the topography of the nanowires. For certain configurations, neuronal networks express small world attributes, with enhanced information flows. Moreover, we observed that neurons in these networks condense in superclusters of approximately 200 neurons. We show that the maximum number of cells in a supercluster is limited by the competition between the binding energy between cells, adhesion to the substrate, and the kinetic energy of the system. Remarkably, the supercluster density value of 200 neurons that we have observed in our experiments is the same found in the cortical minicolumns in the cerebral cortex. The *minicolumns* are the elementary computational units of the mature neocortex. They are constituted by a narrow modular arrangement of vertically connected neurons, with 80 to 250 neurons per column. We speculate that the formation of the structure of the brain is guided by the interplay between energy minimization, information optimization and network topology.



Development of combinatorial targeted therapeutic strategies based on nanotechnology for Cerebral Cavernous Malformation disease treatment.

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Cerebral Cavernous Malformation (CCM) is a major cerebrovascular disorder of genetic origin, which affects at least 0.5% of the general population. Accumulated evidence indicates that loss-of-function mutations of the three known CCM genes predispose endothelial cells to oxidative stress-mediated dysfunctions by affecting distinct redox-sensitive signaling pathways and mechanisms, including pro-oxidant and antioxidant pathways and autophagy. Herein, we show a combinatorial treatment based on lipid nanoparticles (IL). Specifically, ILs are characterized by high biocompatibility, drug payload, controlled drug release, solvent-free and easy to scale-up preparation methods, and could therefore be employed for the target nose-to-brain delivery of therapeutic candidates for CCM disease. A preliminary multitarget combinatorial therapy approach based on the formulation of biocompatible ILs loaded with distinct therapeutic candidates for CCM disease, including avenanthramide, rapamycin and bevacizumab, has already been carried out, obtaining promising results, thereby representing a promising strategy for the effective treatment of this disease. The future aim is to load distinct potential therapeutic candidates in nanocarriers that will be delivered nose-to-brain in a CCM mouse model, which will represent a potential original step toward precision nanomedicine aimed at CCM disease treatment. This possibility is strongly supported by preliminary data demonstrating that lipid nanocarriers are able to accumulate in brain vessels, isolated through capillary depletion method, after intranasal administration of fluorescently labelled lipid nanocarriers in animal models. Indeed, intranasal administration minimizes the toxicity resulting from intestinal uptake and hepatic metabolism, also avoiding the accumulation in non-target organs and tissues, and increasing the drugs bioavailability proximally to the BBB.

Biogenerated Silver nanoparticles: promising antitumoral drugs for cancer therapy

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Silver nanoparticles (AgNPs) are versatile agents with a variety of applications, especially in biomedicine as drug and gene delivery compounds. We used a biogenerated AgNPs embedded into a specific polysaccharide (EPS), by *Klebsiella oxytoca* DSM 29614 under aerobic conditions to induce and study the mechanisms of toxicity in a breast cancer cell line. We found that the cellular responses to AgNPs-EPS exposure represent the sum of events triggered by a direct effect of the cellular uptake of AgNPs, as verified by TEM analysis, induction of intracellular ROS and an indirect effect of free Ag⁺ ions released mainly in mitochondria and secondarily in the nuclei, where they interact with DNA. The treatment with AgNPs-EPS induced morphological and biochemical changes in the cells, consistent with the induction of autophagy and secondarily of apoptosis, as suggested by the upregulation of lysosomes, autophagolysosomes and acidic vesicular organelles, the down regulation of AKT, p-AKT, HSP90 and p62 the increment of ATG5, ATG7 and beclin-1 and the conversion of LC3-I to LC3-II. Proteomic analysis highlights important pathways involved in the mechanism of action of AgNPs-EPS cytotoxicity, such as the endoplasmic reticulum (ER) and oxidative stress. Our results suggest a so-called “Trojan-horse” mechanism, in which AgNPs-EPS internalized within the cells access the mitochondria and nuclei where release Ag ions, which determine oxidative stress and cell death. Further efforts are necessary to analyze the oxidative stress-ER stress-mitochondria connectivity and apoptosis/autophagy.

To cross or not to cross: some, but not all, metal nanoparticles enter cells by plasma membrane direct crossing

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Superparamagnetic nanoparticles (NPs) and, in particular, iron oxide NPs are promising in biomedical applications mainly due to their biocompatibility and customization possibility. This research work investigates the ability of coated and uncoated magnetic NPs to cross plasma membrane bypassing endocytosis. Using *Xenopus* oocytes, we have recently shown that Co₃O₄ and Fe₃O₄ NPs can cross the plasma membrane gaining direct access to the cytoplasm, but also that when these NPs are coated, they lose this ability. Moreover, other metal NPs, such as zerovalent iron and nickel NPs, cannot cross the plasma membrane. Understanding the mechanism and controlling the permeation could open new possibilities in the use of these already valuable tools in nanobiomedicine.

To this aim, we have further investigated the membrane biophysical parameters of the oocytes exposed to different metal NPs by two electrode voltage clamp. Cobalt and iron oxide NPs caused a significant decrease in resting potential and membrane resistance. These can be explained as a membrane leakage occurring when NPs cross the membrane. We think that Co₃O₄ and Fe₃O₄ NPs transiently open a permeation pathway for a non-selective flux of ions that cross the cell membrane according to their electrochemical gradient. On the contrary, oocytes exposed to metal NPs that are not able to permeate the membrane did not change their biophysical parameters.

The possibility to follow NP permeation through the membrane by electrophysiological techniques will be of help in testing ad hoc modified NPs for their ability to cross plasma membranes.

Protein responses in eukaryotic cells exposed to cadmium sulphide quantum dots

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The increasing use of cadmium sulphide quantum dots (CdS QDs) enabled products is expected to be accompanied by their release in the environment. In this study *Saccharomyces cerevisiae* was used as a model eukaryote to study protein modulations by 2D - SDS PAGE (Two Dimensional- Sodium Dodecyl Sulphate PolyAcrylamide Gel Electrophoresis) and gel-free iTRAQ (Isobaric Tag for Relative and Absolute Quantitation) proteomics following cell exposure to CdS QDs for 9 and 24 h. Key proteins involved in essential biological pathways were downregulated, in particular after 24 h exposure. These include the major proteins of the glycolytic pathway as well as mitochondrial components of complexes III, IV and V involved in the oxidative phosphorylation chain. The expression of HSC82 (ATP-dependent molecular chaperone HSC82) and other proteins responsible for protein folding and ubiquitination within the endoplasmic reticulum was also modified. Some of the proteins whose expression was altered have previously been described as strongly-adsorbed proteins at the CdS QDs nanomaterial surface, and involved in the cytotoxicity of these engineered nanomaterials. From an ecotoxicological perspective, the use of *S. cerevisiae* as a model organism sheds light on the impact nanomaterials have on the biochemical responses of the exposed host. These data may be extrapolated to broader contexts and a wider range of organisms.

Dye Doped Silica Nanoparticles as Organized Systems for Nanomedicine

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Silica nanoparticles are versatile platforms with many intrinsic features, including a low toxicity. Their proper design and derivatization yield particularly stable bright nanosystems displaying multiple functions,¹ which can be used for either optical and photoacoustic imaging² and for photoluminescence (PL) and electrochemi-luminescence (ECL) sensing.³ In addition, silica nanoparticles can also be used for as platforms for photodynamic and photothermal therapies.² For these reasons, silica nanoparticles already offer unique opportunities, and further improvement and optimization can substantially expand their possible applications in fields of high impact, such as medical diagnostics and therapy, environmental analysis, and security.

In this context, we have developed a direct micelle assisted strategy based on the use of Pluronic F127 as high molecular weight surfactants. The one-pot synthesis yields PEGylated silica nanoparticles endowed with very high monodispersity, colloidal stability and core-shell structure. These nanoparticles were recently reported with the acronym PluS NPs (Pluronic Silica NanoParticles). These NPs had a silica core of about 10 nm and an overall hydrodynamic diameter of about 25 nm. Interestingly, PluS NPs can be tailored for optimization of processes such as directional energy transfer, which provide those systems with extremely valuable functions: high light-harvesting capability, signal-to-noise maximization, multiplex output, and signal amplification. *In-vivo* experiment proved the absence of toxic effects on mice even after three months after injection. We also found that cellular uptake was influenced by nanoparticle functionalization while the drug loading ability can be tuned with a suitable choice of the silica precursor.

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Engineering Shape of Nanoparticle-Based Magnetic Resonance Imaging Contrast Agent

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To detect and localize cancer in early stage, Magnetic Resonance Imaging (MRI) is used as a noninvasive cancer diagnostic [1]. This technique, suffers from low sensitivity which can be overcome by using contrast agents (CA). The gold can be exploited to create innovative MRI contrast agents to improve sensitivity and resolution of MR imaging [2].

We have investigated the longitudinal relaxation time (T_1) of irregularly shaped gold nanoparticles. The seed-mediated thermal method was used to synthesize the high-index facets concave cubes Au nanostructures [3]. Concave cube nanoparticles (CCNPs) were functionalized with a thiol-modified Gd³⁺ complex. Gd-CCNPs exhibited a relaxivity of 36.3 mM⁻¹S⁻¹ compared to 5.9 mM⁻¹S⁻¹ for free Gd complex. The relaxivity enhancement is likely a result of the restricted molecular tumbling and therefore increase rotational correlation times of the Gd-chelates after conjugation to CCNPs surfaces.

Interestingly, when Gd-CCNPs are compared to the correspondent Gd spherical nanoparticles with the same size, it turns out that the specific shape of concave cube nanoparticles increases the relaxivity from 20.9 mM⁻¹S⁻¹ (for spherical nanoparticles) to 36.3 mM⁻¹S⁻¹. NMRD profile analysis suggests that this difference in relaxivity is due to a higher number of second sphere water molecules for Gd-CCNPs with respect to the spherical ones. The large contribution of second-sphere relaxivity is due to elongated residence time for water molecules present in the second coordination sphere which is dictated by the concave surface of nanoparticle.

In conclusion, we have introduced the novel and efficient Gadolinium based contrast agent for MR Imaging by anisotropy Gold nanoparticles with noteworthy longitudinal relaxivity.

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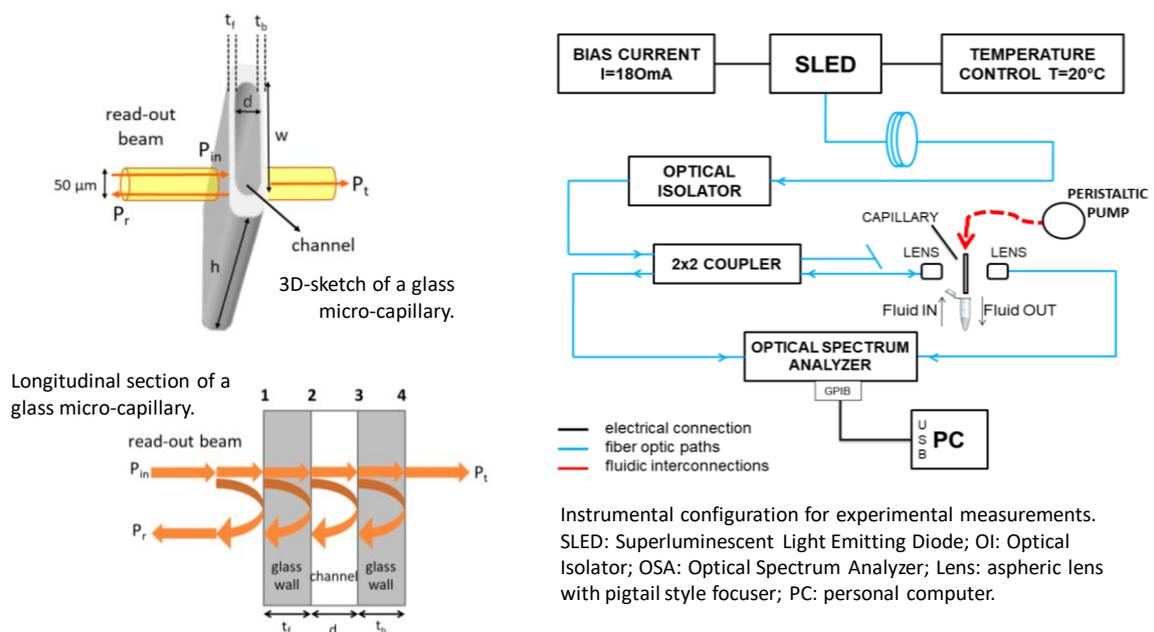
Micro-capillary refractive index sensor based on monitoring of T/R ratio spectral shift

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We have demonstrated a flow-through label-free refractive index sensor for detecting the concentration of water-glucose solutions. The core devices of this opto-micro-fluidic sensing platform are low-cost commercially available rectangular glass micro-capillaries that have been selected for this application with channel depth of 50 μm and 30 μm . By illuminating the capillary with a Superluminescent Light Emitting Diode (SLED), a broadband source with central wavelength emission at $\lambda \sim 1.55 \mu\text{m}$, both the transmitted (T) and reflected (R) optical power spectra from the capillary are detected with an optical spectrum analyzer (OSA), exploiting an all-fiber setup. The selected instrumental configuration and detection method allow remote non-invasive analysis of ultra-small volumes of liquid samples down to 100 nanoliters. Monitoring the spectral shift of the ratio T/R in response to increasing concentration of glucose solutions in water we have obtained the calibration curves of the sensor with sensitivities up to 530.9 nm/RIU (RIU: refractive index unit) and limit of detection (LoD) of the order of $35 \cdot 10^{-6}$ RIU, corresponding to about 1500 μM . Experimental results well agree with the theoretical simulations obtained by modelling the micro-capillary as an optical resonator composed by a sequence of three Fabry-Pérot etalons: front glass wall – inner channel – back glass wall. After the demonstration of amplitude detection at a single wavelength, we finally discuss the impact of the capillary parameters on the sensitivity.



5D printing nano-ladden scaffold for personalized medicine

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Chronic lower extremity peripheral arterial disease (PAD) is a manifestation of systemic atherosclerosis and one of the main causes of loss of walking ability. Due to its advantages, at least in the short-term, balloon angioplasty represents, at present, the most commonly used treatment for PAD. Important advances developed in endovascular technologies address a great variety of anatomic challenges, current and future efforts are directed toward improving long-term patency rates. The 5D printing incorporate data used to create 3D models in addition to data regarding physiological activity for personalized therapy. Moreover, additive manufacturing technology could revolutionize the personalized medical pre-operative management due to its possibility to interplay with computer tomography (CT). We elaborated the CT high-res scan derived from a human PAD and we reconstructed the 3D model of the vessel in order to obtain and verify the additive manufacturing processes. Then, based on the drug-eluting balloon selected for the percutaneous intervention, we reconstructed the biocompatible eluting-freeform coating containing 40nm fluorescent nanoparticles (NPs) by means of rapid freeze prototyping printer and we tested the in-vivo practicability by introducing the 5D high-resolution geometries with NPs-enriched coating in a rat's vena cava, displaying the presence of NPs in the vascular cells. The coating, dissolved in a few minutes, releasing the NPs which are rapidly incorporated in the tissue. We also performed in-vitro studies on VSMC and HUVEC developing a 5D high-resolution geometries with nanoparticles able to dissolve itself with the perspective to apply this method to the personalized medicine.

Dual emitting CdSe/CdS nanocrystals hosting core- and shell-based excitons for last-generation nanotechnologies and as platform for fundamental investigations

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Two-color emitting colloidal semiconductor nanocrystals (NCs) are of interest for a variety of photonic applications such as multimodal imaging, gas sensing, lasing, and integrated photovoltaics. This feature has been achieved by so-called dot-in-bulk (DiB) NCs consisting of a small, quantum-confined CdSe core embedded in an ultra-thick, bulk-like and polytypic CdS shell. DiB NCs can sustain two distinct types of excitations (core and shell excitons) under low optical or electrical excitation,¹ used to produce efficient, multicolor, single-emitter LEDs. Owing to the different exposure to the particles surfaces, the sensitivity of the core- and shell-excitons to local chemical environment are markedly different, which has been exploited in ratiometric probes of oxygen pressure, intracellular pH in living human cells, and in the context of artificial retina applications. In addition to their high potential for practical applications, the outstanding capability to host carriers in both the core and shell regions opens opportunities for fundamental studies on complex excitonic quasiparticles. In this communication, I will report that the tendency of thick-shell CdSe/CdS NCs to photocharging introduces a long-lived resident electron delocalized across the entire NCs, capable of efficiently and alternately interacting with both core- and shell-localized excitons, forming emissive, negatively-charged particles (trions).² Circularly-polarized photoluminescence experiments at cryogenic temperatures (T~3.5K) and high magnetic fields (B≤60T) provided fundamental investigation of the core and shell trions' spin dynamics paving the way for the application of DiB NCs in spin-based nanotechnologies.

¹Pinchetti V. et al., *Nano Lett.*, 10, 6877

²Pinchetti V. et al., *Nano Lett.*, *Just Accepted*

Nanomedicine: is there plenty of room for ethics?

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Emerging technologies, such as nanotechnology and nanomedicine, have brought countless benefits but also several ethical dilemmas. Although every analysis starts by finding a solution for a single problem, an organic approach would be more suitable in this case. In our presentation we will propose three key elements for the decision-making process in nanomedicine: the specific features presented by nanotechnology-enabled products, the fields of application, and the impacts of such products from a quantitative (human health, environment, and economy) and a qualitative (society and human identity) perspective. Our ethical assessment is influenced by the four principles of medical ethics, the precautionary principles, the cost-benefit analysis, and the principle responsibility by Hans Jonas. No unique ethical issues have yet been found in nanomedicine, consistent with the literature. However, the identification of these three key factors allows a holistic ethical analysis and simplify the final evaluation and justification. This method allows the identification of those areas that perfectly respects several ethical principles suggesting that investments in such areas are justified and desirable.

Quality and completeness of physicochemical data for safety assessment of nanomaterials

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Safety evaluations of nanomaterials rely on the availability of adequate and reproducible data on their physicochemical properties. This information is fundamental at different stages, for example nanomaterial identification, prediction of their (eco)toxicological and environmental behaviour, assessment of similarity when grouping and read-across is applied in a regulatory context or when safety aspects are considered in the design phase of new materials. Therefore, having access to repositories where physicochemical data are reported according to standardised formats, stored, curated and made available for re-use is key to generate new knowledge and support regulatory processes in nanosafety. A number of EU-funded research projects have extensively contributed to such advancement. In NANoREG and GRACIOUS, Excel® templates for data logging were developed to harmonise the way test results on nanomaterial properties are recorded. Based on these templates, GRACIOUS developed a procedure for quality and completeness evaluation of existing physicochemical data, including those stored in the eNanoMapper database. At the same time, development of international standards and test guidelines is ongoing to guarantee quality and regulatory acceptance of experimental data on nanomaterials. For instance, the Organisation for Economic Co-operation and Development's Working Party on Manufactured Nanomaterials (OECD WPMN) has several activities aimed at harmonising methods for the determination of properties such as dissolution rate, particle size distribution, (volume) specific surface area, and hydrophobicity. All these tools will contribute to increase data quality and completeness in public repositories and ensure reproducibility, comparability and re-use of data for nanosafety according to FAIR (Findability, Accessibility, Interoperability, and Reusability) principles.

Carbon nanotubes/proteins hybrid for Organic Electronics

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Integration of carbon nanotubes (CNTs) with biological systems such as peptides, proteins and DNA is an emerging and innovative research field with several promising applications. The resulting hybrid architectures combine the mechanical robustness and electronic transport properties of CNTs and the biological features (e.g. molecular recognition, enzymatic properties, amphiphilic behaviour) of proteins and peptides.

In this work, (6,5) semiconductive single-walled CNTs are assembled with lysozyme and are tested in a Electrolyte-Gated Organic Transistor (EGOT) architecture: lysozyme-CNTs dispersion in aqueous solution are drop casted on interdigitated metal electrodes on silicon substrate. The electrical performances of the device and the morphology of the resulting semiconductive layer are analysed. Correlation between EGOT performances and CNT-lysozyme concentration is tested. The retention of functionality of the bound protein is checked with a standard lysozyme inhibitor molecule, 3-N-acetyl glucosamine (NAG3). This work shows how protein-CNTs hybrids open new possibilities for solvent-free production of organic electronics devices and development of new biosensor architectures.

Diagnostic and theranostic implementation of dye-loaded peptide-functionalized inorganic nanoparticles targeting integrin-expressing cells

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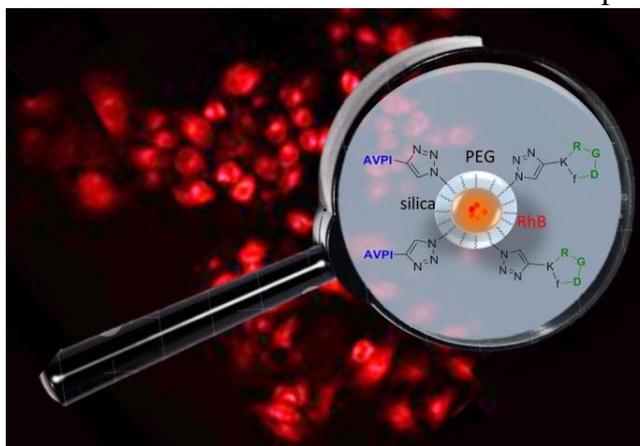
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Integrin are adhesion receptors that mediate cell-cell and cell-ECM interactions, and regulate various cellular functions, including adhesion, migration, invasion, proliferation, apoptosis and anoikis. Besides, integrins are overexpressed during the progression of several diseases, in particular cancer, thrombosis, inflammatory and autoimmune diseases, etc. Hence, interest has recently focused on the construction of integrin-targeted conjugates with drugs, diagnostic probes, nanoparticles (NPs), or nanocarriers, for therapy or imaging.

In the field, we designed nanostructured devices constituted of self-assembled monolayers (SAMs) of disk-shaped zeolite L nanocrystals coated with peptide ligands of $\alpha\beta3$ integrin, to the rapid detection of cancer cells. When challenged with a mixed population of cancer and healthy cells, the peptide-SAMs showed exclusive adhesion of the cancer cells upon very rapid incubation, a feature which is expected to favor the implementation to diagnostic device. Subsequently, aiming at exploring new methods for monitoring the course of the inflammatory processes, we designed peptide-SAMs capable to reproduce the high-density multivalency binding between the $\alpha4\beta1$ integrin-expressing cells of the immune system, and the ligands overexpressed on the endothelial cells in the proximity of the sites of inflammation. Finally, we designed integrin-targeting dye-doped PEG-silica NPs mimicking the proapoptotic protein SMAC/DIABLO.

At low microM concentration, the NPs showed significantly toxicity towards cancer cells, correlated to integrin-mediated endocytosis, without influencing non integrin-expressing cells.



FePO₄ nanoparticles produced by an industrially scalable continuous-flow method are an available form of P and Fe for cucumber and maize plants

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Nanomaterials are widely used in medical and pharmaceutical fields, but their application in plant nutrition is at its infancy. Phosphorous (P) and iron (Fe) are essential mineral nutrients limiting in a wide range of conditions the yield. Phosphate and Fe fertilizers to-date on the market display low efficiency (P fertilizers) and persistence in soil (Fe fertilizers) and negatively affect the environment. In the tentative to overcome these problems, we developed a continuous industrially scalable method to produce FePO₄ NPs based on a rapid mixing of salt solutions in a mixing chamber. The process, that included the addition of citrate as capping agent allowed to obtain a stable suspension of NPs over the time. The NPs were tested for their effectiveness as P and Fe sources on two hydroponically grown crop species (cucumber and maize) comparing their effects to those exerted by non-nanometric FePO₄ (bulk FePO₄). The results showed that FePO₄ NPs improved the availability of P and Fe, if compared to the bulk FePO₄, as demonstrated by leaf SPAD indexes, fresh biomasses and P and Fe contents in tissues. However, nutrients availability is strongly influenced by the crop species used. The particles size affected P availability more for cucumber plants, while in maize the material's size affected more Fe availability. TEM observations revealed that FePO₄ NPs did not enter into the roots, suggesting as delivery mechanism the dissolution in the apoplast. The results open a new avenue in the application of nanosized material in the field of plant nutrition and fertilization.

Microparticles Embedding CaP Nanoparticles for Heart Targeting by Inhalation: Quality by Design Approach for Dry Powder Composition

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Purpose: The goal was to develop by spray drying (SD) a highly respirable microparticulate dry powder (dpCaPs) able to embed and release the unloaded Calcium Phosphate nanoparticles [1]. The polyalcohol mannitol was selected as a soluble, size protective and safe carrier for microparticle construction [2].

The microparticles carrying NPs have to be inhaled and deposited into alveoli; the embedded CaPs, restored by release from microparticulate carrier dissolution, can be translocated across pulmonary vein for direct transport to heart.

A DoE was applied for understanding the effect of the dispersion composition and spray drying (SD) process parameters on selected CQAs of the microparticles embedding CaPs, to optimize the scale up process.

Methods: The Cubic Central Composite Experimental Design applied required to run eleven experiments. Feed rate (3.5-7.0 ml/min), mannitol concentration (0.5-2.0 mg/ml) and CaPs concentration (0.5-7.0 mg/ml) were the three CPPs investigated. Median volume diameter, residual solvent, Emitted and Fine Particle Dose of dpCaPs were elected as Critical Quality Attributes, together with the size of the restored CaPs in aqueous medium.

Results and Conclusion: The amount of mannitol added to CaP nano-suspension to be dried and the concentration of nanoparticles were crucial for the respirability of dpCaps and size of the restored CaPs. Namely, by increasing the concentration of nanoparticles and decreasing the amount of mannitol, doughnut shapes appeared exhibiting decreased respirability and increased size of CaPs. Mannitol plays a key role preventing the irreversible aggregation of nanoparticles inside the drying droplets, when attractive forces overcome electrostatic repulsion.

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Release of IL-8 from BXPC-3 pancreatic tumor cells influenced by nanostructures

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IL-8 secretion from cancer cells may have a profound effect on the tumor microenvironment¹. In the prospective of an effective tumor treatment is important that therapeutic agent doesn't induce an extra IL-8 up-regulation. This preliminary work evaluated cytokine IL-8 release from BXPC-3 cell line induced through co-incubation with poly-L-lactide-co--poly-ε-caprolactone (PLA-PCL) 70:30 electrospun matrices and iron magnetic nanoparticles (NOOC-007). The goal was to evaluate the immunological reaction. NOOC-007 are proposed for hyperthermia treatment and were combined to electrospun matrices in order to improve their residence time at tumor site. BXPC-3 cells were seeded on electrospun fibers and left to proliferate for 7 days in order to evaluate their viability, IL-8 release and infiltration through the matrices. After 7 days, for the last 24h cells were incubated with NOOC-007 (50µg/ml) in order to also evaluate cell viability behavior and release of IL-8 induced by magnetic NPs. Preliminary results show the same release profile of IL-8 both from BXPC-3 cells and BXPC-3 growth on electrospun fibers (**Figure 1**) with decreased amounts after the first 5 days incubation. The starting amount of IL-8 released from BXPC-3 growth on fibers was a little bit higher and in keeping with acute inflammatory response of cells due to contact with a foreign body. Cells incubated with NOOC-007 didn't show differences in IL-8 release compared to controls, showing no reaction to NOOC-007. Confocal analysis and SEM images show the presence of NOOC-007 entrapped in the fibers network and the absence of cell infiltration through the matrices.

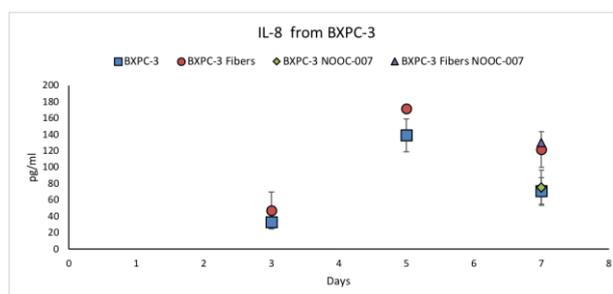


Fig.1 : IL-8 release from BXPC-3 cells

¹ David J.J. Waugh and Catherine Wilson; The Interleukin-8 Pathway in Cancer. Clin Cancer Res 2008;14(21) November 1, 2008

Addressing water scarcity in agriculture: the new frontiers of the in vivo monitoring in open field tomato cultivation

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Drought stress is a major constraint affecting plant growth and crop yield and is worsen by the effects of climate changes. Up to date, 70% of all water withdrawals are employed in agriculture. These changes claimed for new methods for an early detection of drought stress especially in open field. In our research we developed an in vivo textile-OECT sensor, termed as bioristor directly inserted into the plant stem, that allow to monitor continuously and in real time the changes occurring in the ion content of the plant sap. When integrated into tomato plants exposed to drought stress in controlled conditions, it allowed for an early detection of the stress. Here we present two rounds of field tests where bioristor was used to monitor the plant health status during the entire productive season in different water regimes, three in 2018 and five in 2019. Our results showed that bioristor detected for the entire season the changes occurring in sap ion content showing a specific trend in correspondence of extreme drought events, heavy rain phenomena, fruit ripening and the nicotinoids effect. The application of bioristor would allow for water saving up to 36%.

Triplet fusion-based hybrid upconverters: achieving 100% triplet sensitization yield by charge-engineered semiconductor nanocrystals

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Photon upconversion based on sensitized triplet-triplet annihilation (sTTA) exploits the annihilation of metastable triplets of organic emitters to produce high-energy photons. Its efficiency under solar irradiance made it the most promising wavelength-shifting technique to recover the solar spectrum low energy tail to enhance the performance of current photovoltaic technologies for green energy production. Since the application of sTTA upconversion is still hindered by the narrow absorption bandwidth of organic sensitizers, semiconductor nanocrystals decorated with organic ligands have been recently proposed as broadband triplet sensitizers. Upon absorption of non-coherent light, the nanocrystals collect the absorbed energy on the ligands triplet state through a Dexter-type energy transfer. Successively, the ligands act as energy-bridge towards the triplets of free emitters that perform the upconversion. Nonetheless, several factors, competitive with energy transfer, still limit their sensitization efficiency, such as trapping of photo-generated carriers on the ligands themselves. Here we propose a general method for energy transport improvement across the inorganic/organic interface. To drive efficiently the absorbed energy to the ligands triplets, we exploit an intragap state-mediated energy transfer in charge-engineered nanocrystals, realized by doping the semiconductor with electronic impurities. The fast localization of photo-generated holes on the impurity-related electronic level prevents the exciton quenching due to holes extraction, while the preserved energy resonance between the exciton and the ligand triplet ensures a 100% energy transfer yield. Thanks to this efficient energy transport pathway, we achieve an unprecedented upconversion quantum yield of ~12%, which is the current record performance for hybrid upconverters based on sTTA.

Toxicological assessment of food-grade nanoparticles

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Synthetic amorphous silica (SAS) is used in a wide variety of industrial applications including food products. According to the EU specifications, the forms of SAS used as a food additive (E551) include pyrogenic or hydrated silica depending on the process (thermal or wet) used for their manufacture. These processes lead to the production of nanoparticles (NPs) of SAS that interact to form larger aggregates and agglomerates. In this work we have characterized SAS NPs produced by wet route (precipitated silica, NM-200) or thermal route (pyrogenic silica, NM-203) and we have observed that NM-203 exhibits greater cytotoxicity than the precipitated form in a human monocytic cell line differentiated into macrophages (THP-1). To study the molecular interactions of NM-200 and NM-203 in THP-1 cells, we have isolated and identified the set of proteins which are adsorbed with a high level of affinity to the SAS NP surface. These proteins form a so-called “hard corona”, the structure of which defines the biological identity of NPs. We have observed that NM-203 adsorbs on their surface more proteins than NM-200. The hard corona of these SAS NPs was composed of several proteins involved in crucial metabolic pathways: pre- and post-transcriptional modifications, translation, cell motility, molecular chaperoning. These proteins show large unstructured regions that provide high flexibility that promotes their adsorption to SAS NPs. The identification of structural determinants of NP toxicity appears to be essential for a “safety-by-design” synthesis of NPs used as food additives or therapeutics.

Position paper: Update on the EFSA NanoGuidance

Application of nanotechnologies in the agri-food sector: assessment of risks to human health

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In the food sector, applications of nanotechnologies to agricultural production, food processing, and food contact materials are foreseen. Such applications are projected to bring a number of benefits; on the other hand, potential risks have to be assessed and excluded.

The recently published EFSA Guidance for nano-specific risk assessment provides a structured pathway to assess potential risks of engineered nanomaterials and any other type of substance falling under the food law that might present hazards related to the nanoscale. A stepwise framework for nano-related hazard identification and characterisation is outlined in the Guidance to avoid any unnecessary testing.

In the first step, it is investigated *in vitro* whether the nanomaterial degrades to non-nanomaterial forms (e.g. dissolves) under conditions representative of the gastrointestinal tract. Quickly and fully dissolving nanomaterials can be expected not to show nano-related behaviours and thus a standard risk assessment approach may be applied instead of further nanospecific testing.

If the nanomaterial does not quickly and fully degrade, the next step entails gathering any available information from existing literature that meets quality criteria (i.e. that has adequate characterisation data on the nanomaterial tested) and identifying potential hazards through a set of studies, namely (i) *in vitro* degradation test under simulated lysosomal conditions, (ii) genotoxicity tests, (iii) relevant *in vitro* toxicity tests addressing endpoints such as impaired cell viability/cytotoxicity, oxidative stress responses, (pro-)inflammatory responses, and integrity of the gastrointestinal barrier.

If (i) the nanomaterial is non-persistent and (ii) there is no indication of potential toxicity, an argument may be made to waive further nanospecific testing. If this is not the case, a pilot *in vivo* dose finding and ADME study followed by a modified 90-day oral toxicity test should be carried out for identification of the nanomaterials with potential to cause immunological, proliferative, neurotoxic, reproductive or endocrine-mediated adverse effects as appropriate.

Depending on the significance of exposure, and the results of initial toxicological testing, further investigations into chronic toxicity, carcinogenicity, reproductive and developmental toxicity, neurotoxicity, immunotoxicity, allergenicity, endocrine activity, mechanisms and mode of action as well as effects on gut microbiome may be needed.

Poster Communications

Development of chitosan nanoparticles with mucoadhesive/mucopenetrating properties

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Mucus layer is a hydrophilic absorption barrier placed in different regions of the body. The use of nanoparticulate systems take on great importance in drug delivery to mucosal membranes by either prolonging drug residence time at the absorption site (mucoadhesive nanoparticles) or by enhancing diffusion across mucus layer to reach the underlying epithelium (mucopenetrating nanoparticles) [1]. The aim of this study was to design nanoparticles based on chitosan and to evaluate their employment as mucoadhesive and/or mucopenetrating systems for peptidic drug delivery. Nanoparticles were prepared by ionic gelation of chitosan with sodium alginate, sodium carboxymethylcellulose, phytic acid or sodium tripolyphosphate and characterized in terms of size, polydispersity index, zeta potential and drug encapsulation efficiency. Moreover, their mucoadhesion and mucopenetrating ability were investigated by turbidimetric analysis and rotating tube technique [2], respectively. Results showed that nanoparticle sizes ranged from around 150 nm (for sodium carboxymethylcellulose) to around 400 nm (for sodium alginate) with a good polydispersity index. Furthermore, nanoparticles presented a positive zeta potential and the ability to encapsulate vancomycin, selected as a model peptidic drug. Finally, all the developed nanoparticles were able to interact with mucin, thus suggesting good mucoadhesive properties and specifically, nanoparticles based on chitosan and phytic acid showed also the best mucopenetrating ability.

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Novel remotely photoactivated Prussian blue nanoparticles based antibacterial surfaces

A.02

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Antibacterial treatment is an essential issue in many and diverse fields, from medical devices treatment (for example prostheses treatment) to food preservation. To this aim, photo-thermally active nanoparticles can be exploited to develop novel and re-usable materials that can be remotely activated on-demand to thermally eradicate bacteria and mitigate biofilm formation. The antibacterial efficiency of polyvinyl alcohol (PVA) hydrogel films containing non-toxic and highly photo-thermally active Prussian Blue (PB) nanoparticles has been studied upon Near-Infrared (NIR; 700 nm and 800 nm) light irradiation. The local temperature on these PVA-PB films increases rapidly and reaches a plateau (up to $\Delta T \cong 78$ °C) within $\approx 6-10$ s under relatively low laser intensities, $I \cong 0.3$ W/cm². The localized highly efficient increase of temperature on the fabricated films demonstrated significant antibacterial efficacy on both *Pseudomonas aeruginosa* and *Staphylococcus aureus* bacteria. In addition, the localized photo-thermal effect was also sufficient to substantially mitigate biofilms growth.

Nano-formulations of benzophenone and valerophenone thiosemicarbazones for aflatoxins containment and sclerotia suppression in the phytopathogen fungus *Aspergillus flavus*

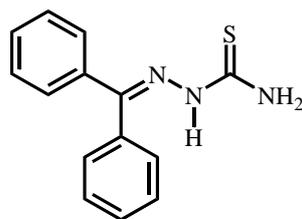
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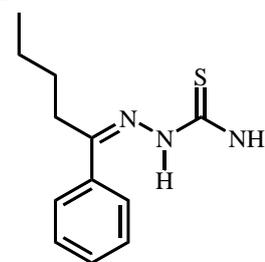
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Nanoparticles are attracting much interest in the agronomical field, since they can be used to target bacteria, fungi and viruses, reducing the use of pesticides, whose abuse is causing a detrimental ecological and environmental impact. Here we report a study on nanoparticles obtained by using poly-(ϵ -caprolactone), chosen for its biocompatibility and biodegradability properties. Poly-(ϵ -caprolactone) nanoparticles were formulated using poly(vinyl alcohol) or Pluronic® F127 as non-ionic surfactant, and then loaded with benzophenone or valerophenone thiosemicarbazone (indicated as **(1)** and **(2)** in figure, respectively) two compounds that inhibit aflatoxin production by *Aspergillus flavus*ⁱ. The nanoparticles were characterized in term of size, polydispersity index, morphology, as well as drug loading capacity. The effects of these nanoparticles on growth, development and aflatoxins production in the aflatoxigenic species *Aspergillus flavus*, a ubiquitous contaminant of maize, cereal crops, and derived commodities, were finally investigated. Aflatoxin production was inhibited to various extents by different concentrations of nanoparticles, but the best inhibitory effect was obtained with respect to sclerotia production: the addition of **(1)** and **(2)** extremely increased the inhibitory effect of both PVA- and F127-NP, resulting in a strong impairing of sclerotia formation. These data support the idea that it is possible to conceive the use of such nanoparticles as an alternative to currently used pesticides for the control of mycotoxigenic sclerotia-forming fungi.



(1)



(2)

ⁱ Bartoli, J.; Montalbano, S.; Spadola, G; Rogolino, D.; Pelosi, G.; Bisceglie, F.; Restivo, F.M.; Degola, F.; Serra, O.; Buschini, A.; Feretti, D.; Zani, C; Carcelli, M. *J. Agric. Food Chem.*, in press, DOI: 10.1021/acs.jafc.9b01814

Interactions with natural biomolecules affect the ecotoxicity Cerium oxide nanoparticles for aquatic biota

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The ongoing development of nanotechnology have raised several concerns regarding the potential risk of nanoparticles (NPs) for the environment, in particular the aquatic ecosystems. In the framework of a need to properly predict environmental implications of NPs, an emerging challenge is to address the complex dynamic of physicochemical and biological processes that drive NPs toxicity once they are released into natural matrices. Therefore the objective of this study was to perform an ecotoxicological evaluation of CeO₂NPs with different surface modifications, representative of NPs bio-interaction with molecules naturally occurring in water environment, to identify the role of biomolecule coating on nanoceria toxicity for aquatic organisms.

Ad hoc synthesis of CeO₂NPs with different coating agents such as Alginate and Chitosan was performed and the NPs were fully characterized. The freshwater species *Daphnia magna* and *Dreissena polymorpha* were used as biological models to test the different ecotoxicity of the CeO₂NPs. Several endpoints were evaluated at different level of biological organization, from the molecular to the entire organism. Overall results show that the different coating affects the hydrodynamic behavior of CeO₂NPs in exposure media. The different coating influenced also significantly the toxic effects of CeO₂NPs in species-specific way. Specifically, in *D. magna* none of the CeO₂NPs triggered a significant oxidative stress, but behavioural assay showed that CeO₂NPs coated with chitosan determined hyperactivity. In zebra mussel the CeO₂NPs coated with alginate seems to behave as ROS scavenger. Our findings emphasize that the eco-corona is able to influence the environmental fate and ecotoxicity of NPs.

A.05

Surface coating with polymeric shells is a valid strategy to reduce metal nanoparticles toxicity? Exemplary studies on alternative in vivo models.

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The use of metal nanoparticles (mNPs) in different field of applications (i.e. Biomedical, manufacturing) is to still today strongly limited by their toxicity towards the biological systems. Surface coating has been already proposed as a promising strategy to reduce mNPs cytotoxicity. Polymer coating, in particular, has been indicated as a powerful approach to increase mNPs biocompatibility, by increasing their stability in physiological fluids and/or reducing their interaction with non-target cells. However, the protective role of polymeric shells on mNPs toxicity is not so obvious and different combinations of polymers and nanoparticles can result in a different outcome on the toxicological effects of these nanoparticles. To face this aspect of nanotoxicology, the use of early developmental vertebrates has proved very useful, with the benefit of reducing time and cost of mammalian models. In this direction, the Frog Embryo Teratogenesis Assay–Xenopus (FETAX) and the FET test on zebrafish (*Danio rerio*), standardized indicators of developmental toxicity, have been recognized as powerful strategies. Exemplary studies based on FET and FETAX, aimed to disclose if and how mNPs toxicity can be reduced by coating nanoparticle surface with different polymeric shells, are here presented. Different types of metal-based nanoparticles (i.e gold and metal oxide NPs) and coatings (i.e. PEI, PEG and PMA) are considered as proof of concept. Altogether, the collected data strongly support the hypothesis that polymeric coatings are able to exert a protective function against mNPs toxicity.

Toxicity of nZn-CuO antibacterial coating on reverse osmosis membranes in zebrafish

A.06

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Among nano metal oxides, Zn-doped CuO nanocomposite (nZn-CuO) showed antibacterial activity more effective than nZnO or CuO nanoparticles, due to higher ROS production. Hence, nZn-CuO is considered a promising nanotool for coating different materials, including reverse osmosis membranes for water purification, to confer antibacterial properties.

However, the effects of nZn-CuO on water purification membranes to the aquatic ecosystem health, when released into the aquatic environment, are still unknown. Consequently, this work aim is to define: 1) the eventual release of nZn-CuO in water and 2) the toxicological potential of nZn-CuO functionalized membranes on aquatic organisms.

Zebrafish (*Danio rerio*) is widely accepted as a model for ecotoxicological studies. Organisation for Economic Co-operation and Development (OECD) recommends the Fish Embryo Acute Toxicity (FET) test (OECD n. 236) to determine toxicity of a wide variety of chemicals on zebrafish embryonic stages. Fertilized eggs are exposed to chemicals for 96 hours and different morphological indicators of lethality are recorded every 24 hours. At the end of the exposure, acute toxicity is determined based on a positive outcome in any of the observations recorded.

During FET test, nZn-CuO affects zebrafish hatching and this effect likely would have an impact on development at later phases. Therefore, FET test is considered a powerful tool to evaluate Zn-doped CuO nanocomposite and reverse osmosis leachate toxicological potential in aquatic environment. Further investigations are necessary to better comprehend the real potential of nZn-CuO as an antibacterial coating for reverse osmosis membrane. Moreover, biomarkers of sublethal effect will be evaluated.

Biogenic silver-iron nanoparticles inhibit bacterial biofilm formation due to Ag⁺ ion release as determined by a novel phycoerythrin-based assay

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Silver nanoparticles (Ag NPs) are antibacterial agents increasingly considered an alternative to antibiotics. The biosynthesis of Ag NPs by bacteria, fungi, algae and plants have received increasing attention due to the need of environmental-friendly technologies. Indeed, bacterial exopolysaccharides (EPS) act as metal reducers and/or NP stabilizers. *Klebsiella oxytoca* DSM 29614 can produce Ag NPs embedded into a specific EPS (Ag-EPS NPs) during growth using citrate as sole energy and carbon source.

K. oxytoca DSM 29614 was cultivated in presence of 0.5 mM of Ag⁺ to obtain Ag-EPS NPs. Since iron stimulates the secretion of EPS, Fe(III)-citrate was used at 0.05 (Low-Fe) or 5 mM (High-Fe), thus, obtaining two kinds of Fe/Ag-EPS NPs. These NPs have a diameter size ranging from 50 to less than 5 nm, as inferred from microscopic techniques, Fourier transform infrared spectrometry and dynamic light scattering. Both kinds of NPs showed a different medium-dependent antimicrobial activities against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. In particular, Low-Fe Ag-EPS NPs were the most effective in terms of minimal inhibitory concentration and inhibition of biofilm formation. These results were correlated with the release of Ag⁺ ions, as it was measured by emission-excitation spectra using a novel phycoerythrin-based fluorescent assay, that was higher for Low-Fe than High-Fe Ag-EPS NPs. So, results prove that Fe/Ag-EPS NPs, produced by *K. oxytoca* DSM 29614, can be considered promising candidates in the development of specific antibacterial and antibiofilm agents.

Lignin@Brochantite as green pesticides: a green approach for the development of bio-based plant protection products.

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Lignin is one of the most abundant plant-derived polymers in nature featured by antioxidant, bactericidal and antifungal properties. Here, the novel materials obtained by combining Cu(II) with technical lignin in basic media are presented. The formed Cu-containing nanocrystalline brochantite ($\text{Cu}_4\text{SO}_4(\text{OH})_6$) were characterized by PXRD and TEM analyses. The dimension varied from a few nm to 200 nm depending on Cu-concentration. Spherical nanocrystals (2-20 nm) formed in the material containing 2% weight, while 10% or 18% weight of Cu led to rod crystals with a thickness between 10 and 30 nm and a length within 50 and 200 nm. To achieve the synthesis of the materials in greener conditions, the use of mechanochemistry was also investigated, by means of a planetary ball mill. Lignin@Brochantite materials were tested for their antifungal and antibacterial profiles against a vast panel of pathogens of agronomical interest. Preliminary tests on tomato plants against *Rhizoctonia solani* were performed, evidencing higher performances than commercial $\text{Cu}(\text{OH})_2$ based product. An important reduction of the amount of copper employed was evidenced indicating a great agronomical potential of these materials.

Unconventional and sustainable nanovectors for phytohormone delivery in plants.

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First developed for biomedical and industrial applications, nanovectors have recently been extended to agriculture, enhancing the effectiveness of crop production agents (i.e hormones, biocides, insecticides), however the use of nanoparticles should be adapted to processes and sustainable materials, while reducing environmental impact. In order to make the process eco-friendly and suitable for the circular economy, we employed waste material such as olive mill pomace and lignin to fabricate nanoparticles. After characterization with DLS, Zeta potential, SAXS and SANS, lipid nanovectors derived from olive mill pomace were loaded with phytohormones (i.e. two auxins, IBA and NAA), to assess the *in vivo* and *in vitro* rooting process in *Olea europaea* cultivars. Lignin nanoparticles were loaded with Gibberellic Acid to evaluate the possible effect on *in vivo* and *in vitro* germination in two model species: *Solanum lycopersicum* and *Eruca sativa*. Nanovector preparation enabled to obtain scalable protocols and stable formulations from olives pomace and lignin to encapsulate phytohormones. Lignin nanocapsules had no adverse effects *in vivo* and *in vitro*, at lignin concentration up to 1% w/v. All the seeds treated with nanocapsules germinated and the seedlings showed tolerance without symptoms of toxicity, moreover anatomy studies evidenced the capacity of lignin nanoparticles to penetrate the tissues of seedlings. Auxin-loaded nanovectors improved the rooting process in cvs Leccino and Leccio del Corno. These results open new perspectives for agrochemical delivery by means of biocompatible methods.

This study was financially supported by Fondazione Cassa di Risparmio di Firenze.

Particle size and concentration and size of nanoceria influence the ecology of *Holcus lanatus* L. and *Diplotaxis tenuifolia* L. DC.

A.10

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The so called “Nano Revolution” with the tumultuous development of nanotechnology and consequent increasing use of new materials in different applications are considered a potential threat for human health but also for the environment. The effects of engineered nanomaterials (ENMs) with the potential risk for living organisms and possible trophic transfer are not so investigated. Released ENMs accumulate into environmental compartments where they can establish complex interactions with the biota. Environmental impacts and effects on plant ecology are almost completely unknown. Cerium oxide nanoparticles ($n\text{CeO}_2$) are among the most widely utilized ENMs in Europe and have a great potential to accumulate and adversely affect the environment owing to their widespread applications in commercial products. A greenhouse factorial pot experiment was carried out to study the response of *Holcus lanatus* L. and *Diplotaxis tenuifolia* L. DC. exposed to different concentrations of $n\text{CeO}_2$ having dimensions 25 and 50 nm, respectively. Plant growth parameters as well as $n\text{CeO}_2$ uptake and bioaccumulation were investigated. Root dry matter and leaf area in $n\text{CeO}_2$ treated plants were higher than in control plants. In a second experiment, $n\text{CeO}_2$ treated plants of *D. tenuifolia* became the food source for the terrestrial isopod *Porcellio scaber* to highlight the potential flow of $n\text{CeO}_2$ along the food web. The effects of presence / absence of $n\text{CeO}_2$ inside *P. scaber* digestion system were studied.]



Synthesis of sugar-based ligands to evaluate the protein-corona formation on gold nanoparticles surface

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Nanoparticle-based drugs have proven to increase the therapeutic benefit of conventional drugs while minimizing side effects [1]. Apart from the enhanced therapeutic effect, nanoparticles (NPs) allow to monitor the physiological response, which will play a significant role in the development of a new era of personalized medicines.

Despite the high expectations, the field of nanomedicine has suffered from several drawbacks that have impaired the translation from laboratory to clinical products. The high surface area to volume ratio of NPs usually results in high reactivity and colloidal instability. This effect is particularly enhanced when NPs come in contact with complex media, such as biological fluids, where their surface forms a nearly irreversible interaction with biomolecules forming a so-called protein corona. Pioneering studies by Dawson et al. [2] have shown that this phenomenon has severe consequences for nanomaterial fate, efficacy and toxicity.

In order to study the stability of this corona, we prepared [3] glucosamide-functionalized gold NPs and investigated their specific interaction with the lectin Concanavalin A (Con A) by means of Fluorescence Correlation Spectroscopy (FCS). In the pursuit of our previous work, we aim to synthesize novel gold NPs coated with mannose, galactose and fucose derivatives to study their interaction with different lectins and provide further insight in the protein corona formation.

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Hi-tech cosmetics by biomass extracts: the use of nanotechnology as the bridge between sustainability and efficiency

A.12

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Nanotechnologies can maximize the performances of a cosmetic product and at the same time allow the optimization of formulation protocols in line with the demands of sustainability. Consumers are increasingly asking for "natural" and eco-sustainable products and nanotechnologies can become a bridge to combine the use of natural raw materials with the optimization of effective and Hi-Tech products.

Our attention was focused on agri-food wastes with particular attention on local biomass (Veneto Region). Biomass are rich of molecules that can be used as valuable ingredients for the formulation of anti-age skin products. The use of biomass derived functional ingredients involves several critical issues concerning in particular their complexity in term of molecular composition and physical features (color, granulometry, smell). The efficiency of these active components was maximized by the use of a Hi-Tech protocol patented (1) by the CATMAT team of the Ca' Foscari University of Venice and valorized by Ve Nice srl, Spin Off of the university. This technology is based on a sustainable and effective sol-gel approach that assures the optimal dosing, bioavailability and efficacy of functional ingredients by the exploitation of the Drug Delivery Systems technology (DDS). A hybrid organic-inorganic network made of polysaccharides, inorganic derivate as silica and acid such as glycolic acid was used as matrix.

The synergy between technology and biomass valorization allows the formulation of a sustainable and high performing product, able to release the active ingredients in a controlled way, guaranteeing at the same time an excellent skin permeation.

1 International Patent Application, PCT/IB2019/053710 (07/05/2019), Michela Signoretto, Elena Ghedini, Federica Menegazzo.

Coating of Cerium oxide nanoparticles with natural molecules modifies the toxic effects towards *Mytilus galloprovincialis*

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In the framework of a need to properly predict environmental implications of nanoparticles (NPs), an emerging challenge is to address the complex dynamic of physicochemical and biological processes that drive NP's toxicity once they are released into natural matrices. In particular this study focused on the effects of surface coating, acquired through the interaction with natural biomolecules, on the behaviour and ecotoxicity of NPs. To this aim CeO₂NPs were *ad hoc* synthesized with different coating agents such as Alginate and Chitosan, two abundant polysaccharides in the aquatic environment. The mussel *Mytilus galloprovincialis* was used as a biological model to test whether these surface modifications could influence NP's fate, uptake and toxicity. Mussels were exposed to 100 ug/L of CeO₂NPs Naked and coated with the two polysaccharides for 7 days and to 1 ug/L for 28 days. A suite of biomarkers related to oxidative stress/damage and energy metabolism was applied. Results showed that the different coating determined different hydrodynamic behavior and stability in water. The coatings affected also CeO₂NPs toxicological outcomes as exposure to CeO₂NPs coated with Alginate triggered oxidative damage, while mussels exposed to CeO₂NPs coated with Chitosan showed increase of antioxidant enzyme activities. Our results highlight that interactions with biomolecules largely present in the aquatic environment could be a driver of NPs' toxicity.

Antibacterial Polyurethane-based Composites: A Comparison between Different Preparation Methods

A.14

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Many medical devices like catheters, dynamic stent or different probes are meant to be used in the human body for different residence times. Nowadays, introducing an antibacterial agent and prolonging its effect for the entire application period results to be one of the main challenges. For this reason, new devices, able to minimize resilient infections and avoid compatibility problems related to excessive release of foreign substances in the body, are the ultimate goal. Within this research project, we studied and developed materials for the realization and / or implementation of biomedical probes with specific antibacterial functions. Thermoplastic Polyurethane Elastomers (TPUs) based composites, containing various known antibacterial functions, i.e. Silver, Silver Nanoparticles, Titanium Dioxide and Chitosan were prepared. The fillers were introduced by two different strategies: processing techniques (melt compounding) or post-processing (coatings). A direct comparison between materials prepared differently allowed to determine strengths and weaknesses of their final properties and their influence on the physical-mechanical and antibacterial properties of the starting polymeric material.

Acknowledgment

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Development and characterization of astaxanthin-containing whey protein-based nanoparticles

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Astaxanthin (ASX) is a carotenoid of great interest due to its potential health benefits but its use in the food, feed and pharmaceutical fields is limited due to low bioavailability, scarce stability to thermo-chemical treatments, susceptibility to oxidation, and poor organoleptic characteristics. The aim of this work was to develop a method to stabilize astaxanthin extracted from the microalgae *Haematococcus pluvialis* (*H.p.*) and to improve its nutritional and functional properties through nanoencapsulation. Nanoparticles (NPs) were produced by emulsion solvent-evaporation technique starting from *H.p.* oleoresin using whey proteins concentrate (WPC) as stabilizer. The efficiency of encapsulation was 96%. The particle size (*Z*-average) was in the range of 80-130 nm and the superficial charge (measured as zeta-potential) was negative (-20-30mV). The stability of the NPs upon resuspension in water was assayed through a panel of stress tests, i.e. extreme pH, UV-radiation, Fe³⁺ exposition and heating at 65°C, that showed always a superior performance of encapsulated ASX in comparison to the oleoresin, even if at pH 3.5-5.5 NPs tend to precipitate. Simulated gastroenteric digestion conducted to study the release of ASX in physiological conditions, showed a maximum bioaccessibility of 76%, with 75% ASX converted into the more bioavailable free form. The data collected suggest that NPs might have possible future applications as supplements for human and animal diets.

New π -delocalized [Pt((N[^]C[^]N)Cl) (N[^]C[^]N= 1,3-di(2-pyridyl)benzene) complexes with interesting luminescent properties.

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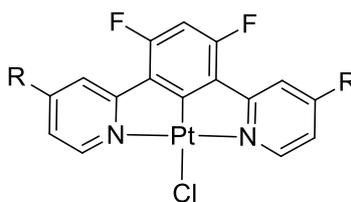
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There has been a growing interest in the design of luminescent transition metal complexes as phosphors for Organic Light Emitting Devices (OLEDs) over the past decade^{1,2}. Though the field has to date been dominated by iridium(III) complexes, platinum(II) complexes attract nowadays increasing interest. Pt(II) complexes with terdentate ligands based on cyclometallated 1,3-di(2-pyridyl)benzene (dpyb), which offer the metal ion an N[^]C[^]N coordination environment, are amongst the brightest Pt-based emitters in solution at room temperature³. Remarkably, the emission color of OLEDs based on these complexes can be easily tuned changing the substituents on the terdentate ligand³. Some of us have described the effect of the incorporation of ArC=C– and ArC≡C– substituents at the central 5-position of the phenyl ring of dpyb^{4,5}. Now, we report new Pt(II) terdentate complexes with different π -delocalized ligands in *p*-position of the pyridine rings of dpyb with interesting luminescent properties (see figure).



R = Me, PhNPh₂, Mesityl

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Polymer-based water-processable blend nanoparticles as a tool to improve OPV sustainability

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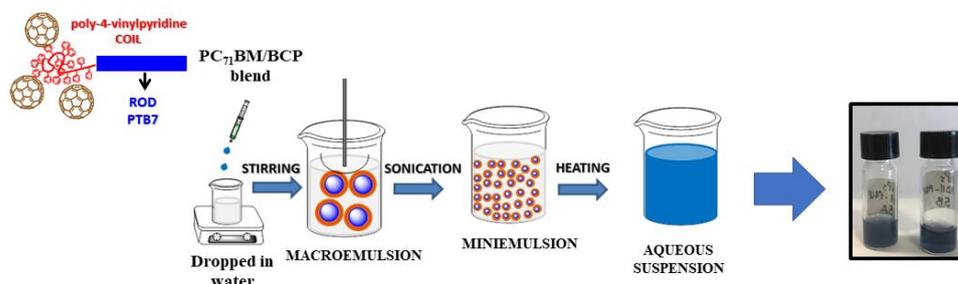
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Organic photovoltaic (OPV) technology has been intensively investigated over the last decades as it represents an intriguing alternative for electrical power generation. Nevertheless, its market penetration is limited not so much by the lower power conversion efficiencies compared to inorganic devices, but rather by the use of halogenated organic solvents, which are toxic and harmful (1-5).

Polymer-based water-processable nanoparticles (WPNPs) represent a way to overcome the problem. Amphiphilic rod-coil block copolymers (ABCs) (6), bearing a rigid block and a hydrophilic flexible segment, are able to self-assemble *via* miniemulsion method without using any surfactant, generating organized nanostructures. The hydrophilic flexible block works as surfactant and interacting with aqueous medium assures the colloidal suspension stability (7). Also, it interacts with the electron-acceptor material (n-type), leading to the formation of pre-aggregated domains, suitable to achieve the charge percolation into the final device.

Particularly, we synthesized the low band-gap polymer PTB7, in order to connect it to a tailored segment of P4VP producing a new ABCP, the PTB7-*b*-P4VP. This polymer allows the fabrication of efficient PV cells and furthermore it is semi-crystalline (9). We carried out an in-depth characterization to confirm the molecular structure of PTB7-*b*-P4VP, and we tested its capability to self-assemble in aqueous medium to produce nanoparticles, both neat and in blend with fullerene derivatives. The obtained WPNPs were characterized by DLS and spectroscopy, deposited in films characterized by AFM and will be employed as active layer in OPV devices.



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Determining the thickness of van der Waals crystals by Raman spectroscopy: the case of black phosphorus.

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Two-dimensional materials obtained by exfoliation techniques from van der Waals (vdW) crystals have captured an increasing scientific interest. Among them, few-layer thin black phosphorus (BP), known as phosphorene, has recently gained a lot of attention being one of the few mono-elemental vdW materials capable of supporting devices[1], [2]. The large foreseeable use of BP in nanotechnology demands for fast and reliable methods for its thickness determination. This is crucial when dealing with the case of a large quantity of exfoliated flakes which suffer of air-degradation problems[3], [4].

In this work we developed a method for the determination of the thickness of mechanically exfoliated BP-flakes with more than 10 layers. In our methodology Raman spectroscopy is used to measure the thickness of BP flakes with silicon as a reference material for intensity calibrations. By combing Raman and AFM measurements we obtained an intensity-calibration curve which determines the thickness of a BP-flake in the range between 5 and 100 nm with an accuracy of about 20%. We also tested the reproducibility of the method on two different setups finding similar results.

This method is at the grasp of any lab with the possibility of making a Raman spectrum. The methodology is also open to a generalization to other vdW materials with a band characterized by the same Raman tensor of BP. We believe that it could be of future use in any work requiring further processing and thinning of vdW materials down to their extreme 2D limit.

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A comparison between Broadband Ferromagnetic Resonance techniques for the characterization of magnetic multilayers

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Over the last decades, the deep understanding of the magnetic multilayers properties played a central role in the context of spintronics, mainly due to their use for the implementation of ultra-fast and ultra-low power Magnetic Random-Access Memory (MRAM) devices. The Ferromagnetic Resonance (FMR) technique allows to extract the most important parameters which describe the dynamic behavior and the equilibrium configuration of the magnetization inside a ferromagnet (FM). In this contribution a comparison between two different broadband FMR setups has been performed: one based on a Vector Network Analyzer (VNA) and another on a microwave source and a power meter detector. In order to excite the FMR precession inside the FM layer, a Grounded Coplanar Waveguide (GCPW) has been used to lead the microwave signal to the measured samples. The setup composed by power meter and microwave source turned out to be the best solution in terms of source stability, ease of use and higher signal-to-noise ratio. In particular, two samples composed by evaporated polycrystalline nickel (Ni) layers, with thicknesses of 60 nm and 15 nm, grown on top of 10 nm thick sputtered platinum (Pt) layers have been analyzed. As a result, besides the FMR signal, the spectrum of the thicker Ni(60 nm)/Pt sample showed the presence of a second peak which has been attributed to the presence of Standing Spin Waves (SSW) inside the Ni layer. The analysis of the SSW signal has allowed to determine the exchange stiffness constant of the Ni layer, further confirming the FMR technique versatility.

Innovative Chiral Materials and Media for Enantioselection in Chiral Electrochemistry and Advanced Applications in Spintronics

A.20

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The highest degree of selectivity in electrochemical recognition is achieved with enantioselective electroanalysis, implying the ability to discriminate specular images of a given electroactive molecule [1]. Unprecedented enantioselective recognition in terms of large potential differences was recently observed in analytical experiments by our research group[2], implementing:

- 1) enantiopure electrode surfaces based on inherently chiral films (with different stereogenic elements, C_2 axis vs helix);
- 2) enantiopure media based on inherently chiral (or simply chiral) ionic liquids [3,4];
- 3) Deep Eutectic Solvents (DES), commonly defined as systems composed of a mixture of at least two components, a hydrogen bond acceptor and a hydrogen bond donor.

An even more striking feature implying inherently chiral films was obtained in the frame of the CISS (Chiral Induced Spin Selectivity) effect, recently unveiled by Ron Naaman and co-workers [5]. In this frame we present an innovative set-up which includes *i*) a non-ferromagnetic electrode (ITO) modified with a thin electroactive chiral film, *ii*) achiral redox couples and *iii*) an external permanent magnet. A spectacular unforeseen effect was observed, in fact CV peaks reveal an impressive potential shift by flipping the magnet orientation (north vs south) [6].

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Effect of the structure of the Zinc-based curing activator on the mechanical behavior of rubber nanocomposites

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The crosslink density and distribution inside the polymer matrix affect the mechanical properties of rubber nanocomposites (NCs), arising from the use of reinforcing filler combined with the formation of sulfur bridges between the polymer chains promoted by the vulcanization process.

Activators and accelerators are used to improve the vulcanization rate and among them ZnO is the most used, due to its capability to reach high kinetic and crosslinking efficiency.

Since the catalytic activity of Zinc has a central role in the formation of crosslinks, this study focuses on the effect that the structure of the catalytic sites and their localization inside the polymer matrix have on the mechanical behavior of rubber materials. To do this, a new highly efficient activator, Zn@SiO₂ based on zinc single sites anchored onto the silica surface, is used as double function filler, acting as both activator and reinforcing filler.

The mechanical properties of rubber NCs prepared with Zn@SiO₂ are compared to NCs conventionally cured with ZnO particles. By performing DMA (Dynamic mechanical analysis), Uniaxial tensile test and the fracture test, different mechanical properties, such as stiffness and fracture toughness, were highlighted, and they were correlated to a higher crosslinking density close to the filler surface, promoted by the localization of the catalytic site on it.

The results suggest that localizing the catalytic sites at different distance from the filler particles dispersed in the rubber matrix is a promising tool to control the crosslinking density and distribution, which means tuning the mechanical properties of rubber NCs.

Self-doped polyelectrolytes for interfacial engineering in inverted organic solar cells

A.22

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Engineering of the organic/electrode interface is a promising approach to enhance the performances of optoelectronic devices, such as OLEDs, organic and perovskites solar cells. The employment of interfacial materials promotes the selection and collection/injection efficiency of the charge carriers.¹⁻³

In this context, polyelectrolytes with ionic pendant groups have received increasing attention as interfacial materials in polymer solar cells.⁴ The ionic group ensures good water/alcohol solubility, fundamental for orthogonal deposition in solution-processed multilayer devices, but also induces interfacial dipoles leading to energy-level alignment at the interface with an improved hole/electron selectivity. Moreover, a suitable chemical design can result in a self-doping behavior, either p-type or n-type, that promotes the hole or electron transport, respectively, to the anode and cathode electrodes.

One of the current requirement to get closer to the industrial scale-up is the development of solution-processable functional materials for inverted geometry device, consisting of a bottom transparent cathode and a top anode electrode.

In this view, we have designed and synthesized novel water-alcohol soluble interfacial materials granting self-doping behavior, suitable for inverted device applications: (i) anode modifiers consisting of low bandgap conjugated polyelectrolytes with alkyl-sulfonate groups, designed to ensure a good wettability on the hydrophobic active layer and (ii) transparent ion-containing naphthalene diimide polyelectrolytes to apply as cathode interlayer. The functional behavior of these electrode interfacial materials is herein investigated in inverted polymer solar cell devices.

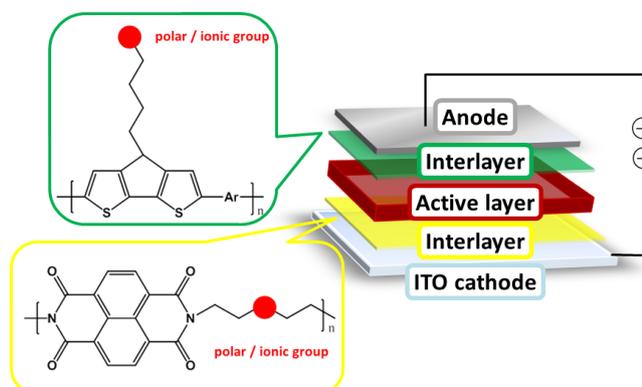


Figure 1: General structure of interfacial materials and scheme of the inverted geometry device.

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Functionalization of carbon nanotubes for nitroaromatic explosive detection

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Carbon Nanotubes (CNT) are considered promising materials for many types of new electronic devices due to their unique electronic structure and electric properties. In particular CNTs provided with suitable functional groups bonded to their surface can be used to reveal different chemical compounds.

CNT based chemiresistors show, for instance, promising performances in explosive sensing. These systems already demonstrated a very high sensitivity in detecting explosives, in particular molecules of trinitrotoluene (TNT), which is a common explosive used in improvised explosive devices (IED).¹ In such nanostructures the signal detection is based on conductance changes.

With the final goal of producing a portable sensors for unmanned explosive detection, we performed the functionalization of the surface of MWCNTs. In particular, we will present our results in the oxidation² and subsequent introduction of amino groups³ on the CNTs surface. These amine units should interact with the electron-poor aromatic ring of TNT.

In order to investigate the effective covalent bonding of functional groups, infrared absorption measurements, elemental analysis and X-ray Photoelectron Spectroscopy (XPS) were performed on the CNTs prepared from the reactions.

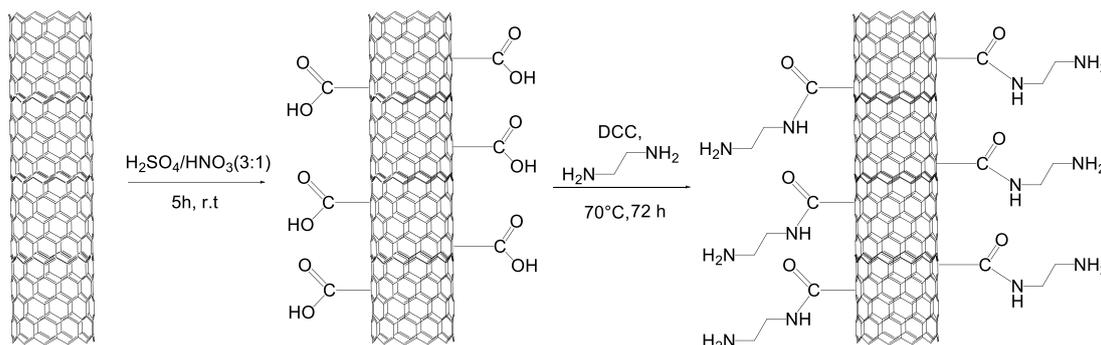


Fig 1: Schematic illustrating to CNTs functionalization

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Co-Polymeric Nanosponges Synthesized from Cellulose Biomass for the Heterogeneous Catalysis of Henry Reaction

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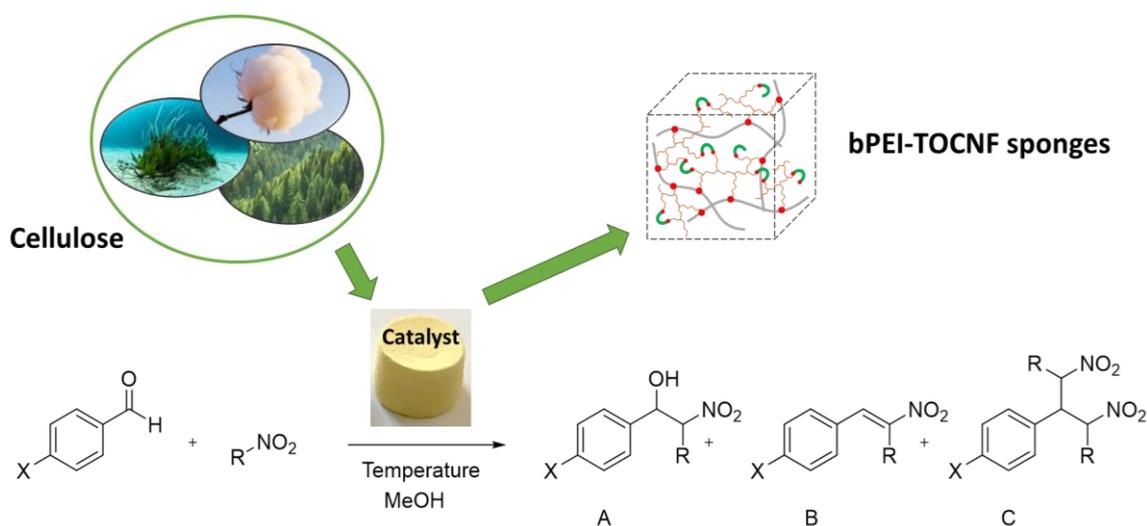
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Functionalized silica materials/nanomaterials have been extensively utilized in heterogeneous catalysis (Wight, A. *et al.*, Chem. Rev. 2002). Nevertheless, nowadays there is an increasing request for the development of alternative heterogeneous catalytic systems, possible derived from biomass discard, but which should be at mean time cheaper, more sustainable according to circular economy principles and as stable as silica materials.

Herein we report micro- and nano-porous aerogels derived from cellulose waste sources, such as recycled paper and *Posidonia*. Cellulose was oxidized, nanofibrilled and thermally cross-linked with branched polyethyleneimine (bPEI), affording a nanostructured material which has been already employed in environmental remediation (Melone *et al.*, ChemPlusChem 2015) and specific ion sensing (Riva *et al.*, ChemPlusChem 2019).

Herein we report how these sponge-like materials behave as ideal catalysts for the Henry reaction, providing excellent yields and a variable selectivity depending on the reaction conditions. In fact, by varying solvent and reaction temperature, we are able to drive the synthesis selectively to the nitro-aldol, the elimination product or the double addition product. These systems have proved to be able to catalyse Henry reaction not only starting from aromatic aldehydes, but also using aliphatic aldehydes and aliphatic and aromatic ketones as reagents.



Electrical characterization of nanoparticles random networks

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Nanoparticles (NPs) random networks can be exploited in electronic devices for unconventional information processing, for example for reservoir computing. A preliminary analysis of the possible materials suitable for this purpose is necessary.

Here we present an electrical characterization of nanoparticles random networks, deposited on a Si/SiO₂ substrates with pre-patterned interdigitated ITO/Au electrodes. In particular the behavior of two different nanoparticles assemblies, manganese-doped lead sulfide (PbS:Mn) and gold nanoparticles (Au), has been investigated.

The functional characteristics of these random networks are determined by the NPs charging energy, which depends on the nanoparticles size and on the dielectric surrounding the nanoparticles. Chemically synthesized colloidal nanoparticles, surrounded by organic capping agents, are in fact employed.

A room temperature electrical characterization of the NPs based devices shows a non-linear IV characteristic in both samples, revealing that the systems are dominated by Coulomb blockade effect. The non-linearity is a fundamental characteristic for the reservoir, which needs to operate as a non-linear mapping.

In the case of gold samples, we analyzed the behavior of nanoparticles with different sizes. Comparing the IV curves, we see how the non-linear behavior is progressively lost as the nanoparticle dimension increases, according to the charging energy values.

In the PbS:Mn samples, a quasi-memristive behavior is also observed. A resistive switching phenomenon is observed when a high voltage is applied for a certain time interval. Pulsed IV measurements reveals an irreversible switching, even if the underlying mechanism is still to be clarified.

Exposure to metal nanoparticles through tattoo inks

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The practice of tattooing can be considered a source of exposure to metal nanoparticles (MNPs, < 100 nm) contained in tattoo inks and related health safety has not yet been clarified. Twenty inks of different brands and colors were sampled in Italy in 2019 and analyzed by Single Particle Inductively Coupled Plasma-Mass Spectrometry (SP ICP-MS) for the determination of size and concentration of MNPs of Al, Co, Cr, Cu, Hg, Ni, Pb, Ti and Zn. NPs of Al were observed in many colours at concentrations between 0.12-2.31 µg/g, both at smaller (62-80 nm) and relatively larger (105-140 nm) diameters. A consistent fraction of inks were constituted of NPs of Cr in the size range 42-62 nm and concentration 0.07 - 1.54 µg/g. NPs of Cu, sized between 44-96 nm, were highly concentrated in green (581-721 µg/g) and blue (492-3287 µg/g) inks. A significant part of inks contained NPs of Zn (range, 26-59 nm) at concentrations 0.10 - 1.59 µg/g. Small NPs of Pb were found with diameters of ca. 27 nm. Titanium particles ranged 166-383 nm. No particles of Co, Ni and Hg were detected in any of the inks. Tattoo practices expose humans to different MNPs, which can lead to skin or systemic toxicity also due to synergic effects of mixtures of MNPs.

Nanomaterials toxicity and cell death modalities

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Nowadays nanomaterials have excellent application in various fields, as cosmetics, chemical industries and biomedicine. However, on the biosafety of these materials there are some studies that pointing out its cytotoxicity.

The potential toxicity of nanomaterials on target organs and cells are mediated by different mechanisms that include disruption of membrane integrity, alteration of protein structures, mitochondrial alteration, oxidative stress, generation of reactive oxygen species (ROS), DNA damage and inflammation. Multiple features of nanomaterials, including their size, shape, chemical composition, surface charge, aggregation rate, adsorption of proteins, released ions, and solubility are the main causes for cell damage. The most common pathways of cell death are apoptosis, necrosis, necroptosis, and autophagy.

Several nanomaterials can trigger intrinsic apoptotic pathway in the cancer cells and the normal ones. The primary mechanism of action is ROS production and mitochondrial damage (Condello et al., 2016).

Some studies shown the contradictory role of nanomaterials in autophagy modulation. It has been demonstrated that nanomaterials can block autophagy inhibiting the lysosomal enzymes function; however, other studies indicated that nanomaterial induced autophagy by mitochondrial disruption. Finally, there are cell models where the cytotoxicity is due to necroptosis induction (Sharifi et al., 2019). These different cell death models can be simultaneously activated and the priority of one is be due to the physical and chemical properties of nanomaterials.

Super hydrophobic surface properties to enhance organic electrochemical transistor selectivity in early cancer detection

B.03

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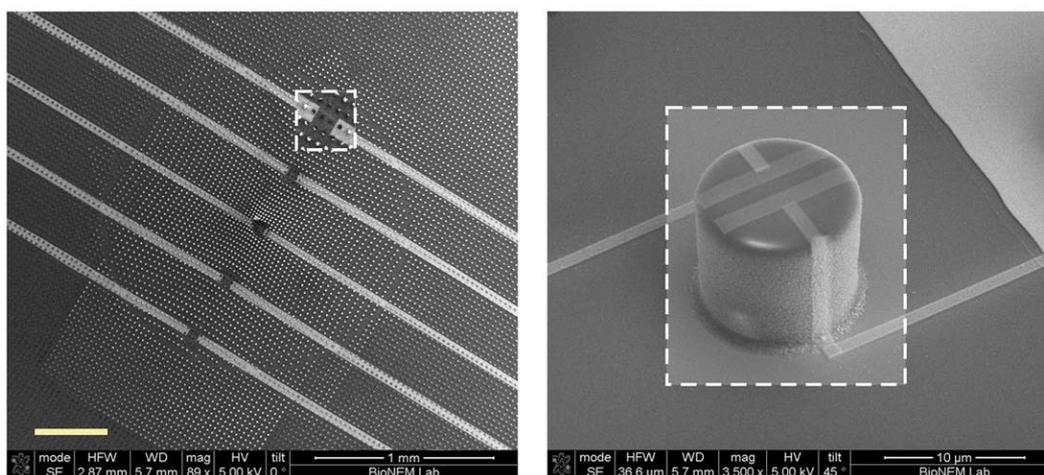
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The ability to control surface properties, in electrochemical sensing devices, is of crucial importance to improve the detection properties and to control the diffusion of analytes in the fluid samples. In recent years the development of organic electrochemical biosensor based on transistor architecture has grown in many applications. Due to the high biocompatibility of the materials, high sensitivity, low cost and flexibility, organic electrochemical biosensors, have been used to detect ionic species in fluids, for example, as wearable devices for biological fluids monitoring, as detection of DNA, neuro-transmitters, and many others. Even if the transistors present a high sensitivity and have the ability to interact with ionic species, the selectivity is limited and related to the introduction of chemical linker to limit the interaction with specific molecules. Here we focused on a different physical approach based on the fine tailoring of surface hydrophobic properties. Thanks to the presence of a micro and nanostructure with concentric pillars and distributed sensors channels, the liquid sample is driven and shaped as a spherical drop and monitored in different local positions. The strong convection forces in the spherical drops and the diffusion properties related to the molecular mass, shape and charge, allows to detect specific sized molecules, and to calculate their distribution in the solute. This approach has been used to determine successfully the presence of cancer cells, respect to healthy samples, in secretome of primary cultures.



NanoBerberine for Alternative Antitumor Therapy

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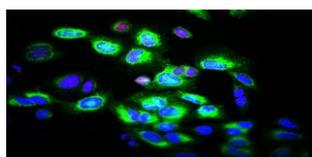
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Berberine is a quaternary ammonium isoquinoline alkaloid isolated from a variety of Chinese herbs. It is endowed with diverse pharmacological activities such as antibacterial, anti-inflammatory, hypoglycemic, antitumor. Berberine is now regarded as an emerging, alternative antitumor drug, due to its high biocompatibility and the multiple mechanisms of its cytotoxic activity including mitochondrial-targeting, antiangiogenic effect, interference with telomerase. However, in spite of these favorable characteristics, the poor aqueous solubility, self-aggregation tendency, pH instability and poor membrane permeability strongly restrain its in-vivo use. Nanoencapsulation may overcome these drawbacks and improve the drug bioavailability either for oral and parenteral administrations. Berberine Nanocapsules (NanoBerberine) have been prepared by a new complexation method providing supramolecular aggregation of the drug-hydroxypropylbetacyclodextrin complex in the presence of polymeric counter-ions like pectins. Nanoencapsulation significantly improved Berberine aqueous solubility. Moreover the mean size, polydispersity, drug encapsulation efficiency and drug loading of the Nanocapsules were all suitable for a size-controlled drug biodistribution in accordance with the Enhanced-Permeability-and-Retention Effect of the drug nanocarriers in vivo (Table 1).

Mean Size (nm)	Polydispersity	Drug Encapsulation Efficiency % (w:w)	Drug Loading % (w:w)	Solubility μM	
				BER	NanoBER
127.5 \pm 7.7	0,238 \pm 0,007	98.02 \pm 1.5	11.06 \pm 0.51	4.05	> 10

In vitro studies on Saos-2 and SH-SY5Y cells treated with NanoBerberine showed cytotoxicity, Ros increase and mitochondrial potential decrease.

Confocal Laser Scanning Microscopy images (Figure1) collected by exploiting the natural fluorescence of Berberine showed NanoBerberine accumulation in the cell mitochondria and around the nucleus. Pure Berberine, on the contrary, did not accumulate in the same conditions. These results indicate that NanoBerberine may overcome the drawbacks of the free drug and provide a tool for an alternative antitumor therapy characterized by therapeutic efficacy without dose-limiting toxicity.



Nanodrugs: dream, (next) future, or even coming reality?

B.05

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When thinking to the perfect drug for better therapy one would like to have a molecule able to be speedily administered just to the very target, without collateral effects nor transit compartments to travel through. Traditionally drugs are instead mostly assumed by ingestion, going to blood through digestion, when not directly injected, and then traveling through the entire body implying quite a lot of collateral effects besides therapy. Nanoparticles could be directly injected and produced in such a way to be minimally toxic while active. It is not easy, as proved by several lack of results in the last few years. But sometimes it could be easier, as shown by a great start up company spinning off from University of Padua, thanks to a young bright lady professor: having discovered a molecule against cirrhosis, the problem was how to administer it: embedding it in sugar and injecting in blood, it travels to liver, eager of both blood and sugar thus locally dissolving the sugar cap and exposing the molecule, healing the cirrhotic liver. Columbus' egg: not a general solution, but a general suggestion: make things as simple as one could hope it works. Other cases may be more difficult, requiring a more complex chemical cap and/or more complex physical transport, but the road is traced, toward a true personalized medicine, considering the very need of each patient and avoiding damaging while trying to heal, as per the ancient Hippocratic Oath!

Lipoplexes for miRNA delivery in myocardial regeneration

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Myocardial infarction is one of the major causes of mortality in industrialized countries. Several strategies have been studied to regenerate myocardial infarction, reaching a limited success [1].

Direct reprogramming of cardiac fibroblasts populating post-infarct scar into cardiomyocytes could represent an alternative promising approach [1-3]. In 2012, mouse fibroblasts transfected with a combination of four microRNAs (miRNAs), termed “miRcombo”, were transdifferentiated into cardiomyocytes [1-3].

In this work, nanotechnology-based approaches were explored to efficiently deliver miRNAs to human cardiac fibroblasts in the perspective of their direct reprogramming. Lipoplexes containing negmiR or miR-1 (miRVana™ miRNA Mimic, Life Technologies) were prepared at different N:P ratios (3.0; 1.75; 0.70; 0.35). Lipoplexes showed an average size between 405 nm and 560 nm and an average zeta potential between +21 mV and -29 mV. Encapsulation efficiency and morphology (cryoTEM) were also analyzed.

In vitro tests with human cardiac fibroblasts showed a significantly higher miR-1 expression in the case of transfection with lipoplexes compared to a commercial agent, as evaluated by digital droplet PCR.

As a conclusion, in this work new lipoplexes were developed showing efficient delivery of miR-1 to human cardiac fibroblasts, for future use in direct reprogramming.

BIORECAR project is acknowledged: it has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme grant agreement No 772168

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Diffusion-limited aggregation models to simulate the self assembly of metal nanoparticles

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Metal nanoparticles (NPs) are of great interest in research and industry owing to their improved physical and chemical characteristics and potential impact in fields such as electronics, medicine, and biomedical engineering. The shape and the size of NPs together with their organization in micro/nanostructures influence their electrical and optical properties, increasing the attention to NP realization methods to create well-defined nanostructures.

We produced gold NP aggregates (Fig.1a) with an overall size in the nano-meter range employing electroless techniques. The relationship between nucleation events, subsequent growth, assembly, as well as the effect of interfacial chemistry of the reducing agents, have been determined by in-detail theoretical model and simulations. We used a diffusion limited aggregation (DLA) scheme to simulate the NPs growth around spherical nanoporous silicon precursors and cellular automata to reproduce the random displacement of gold ions in the domain prior deposition. The aggregate assumes a dendritic structure, with a succession of symmetric/non-symmetric branchings creating a nested tree, similar to fractals (Fig.1b). At the early time of the process, the kinetics of formation of the aggregates is fast, with an initial burst in correspondence of which particle growth occurs instantaneously. After that, NPs continue to growth at a constant rate (Fig.1c), consistently with the experimental results. Moreover, results indicate that the efficiency of growth depends heavily on the particle radius of curvature (Fig.1d). The model provides insight into the geometrical structures that system forms upon aggregation and can be significant in further understanding the molecular self-assembly synthesis of nanostructured particles.

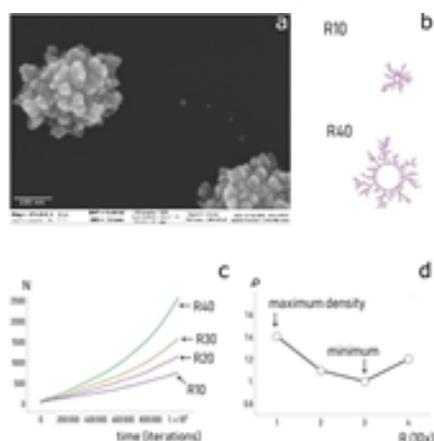


Figure 1. A) SEM micrograph of gold NPs. B) Steady state shape of the aggregates after 1M iterations for the initial radius of curvature R of the seed varying between 10 and 40 pixels. C) Total mass N of the aggregate at a specific time t , for different R . D) Density of an aggregate ρ (i.e. mass to the circumference of the initial seed upon which the aggregate was formed) as a function of R .

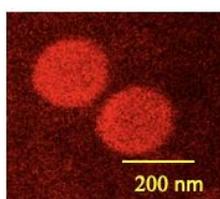
Fenretinide-Nano-Lipoplexes as New Chemopreventive and Non-Toxic Antitumor Agents

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Fenretinide is a semi-synthetic retinoid endowed with antitumor activity on a wide range of tumor types without toxicity to normal cells. This favorable pharmacologic profile is due to its unique mechanism of action involving inhibition of dihydroceramide-desaturase with an increase in dihydroceramides vs ceramides. The consequent alteration in cell glycolipids drives apoptosis in tumor cells but not in normal cells. The lack of toxicity makes Fenretinide particularly suitable to be administered at high doses for long time-periods with the aim to obtain a complete body-sterilization from cancer-cells. These favorable features have prompted many clinical trials, over time, either on pediatric and adult tumors. Unfortunately all of them provided disappointing results because the use of conventional formulations failed to raise the drug bioavailability to the extent required for therapeutic activity. Therefore, new formulations, able to increase Fenretinide bioavailability, are urgently needed to exploit the antitumor potential of this drugs devoid of dose-limiting side effects. We prepared new Fenretinide-Nano-Lipoplexes (Fen-NLpx) by an original procedure including Fenretinide salification with phosphatidylcholine and salt complexation with hydroxypropyl-beta-cyclodextrin (Figure1 and Table1). Fen-NLpx have been tested on a wide range of cancer cell lines. They demonstrated strong cytotoxic activity, always higher than the free drug in all the analyzed cell lines. The in vivo administration of Fen-NLpx, provided antitumor activity in xenografts models highly resistant to conventional chemotherapy. These results indicated the ability of Fen-NLpx to improve Fenretinide bioavailability at the levels required for a therapeutic use of this drug endowed with strong antitumor activity without toxicity.



Mean Size(nm)	Polydispersity	Drug Encapsulation Efficiency % (w:w)	Drug Loading % (w:w)
200.5 ± 11.5	0.306 ± 0.016	97.8 ± 0.3	9.20 ± 1.1

Employment of an argininocalix[4]arene nanosystem for the efficient cell penetration and delivery of peptide nucleic acids

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Peptide nucleic acids (PNAs) are DNA analogues in which the sugar-phosphate backbone is replaced by N-(2-aminoethyl)glycine units. These molecules efficiently hybridize with complementary DNA and RNA, forming both double helices through Watson-Crick base pairing. Thanks to their resistance to nuclease PNA have been proposed for antisense and anti-gene therapy and as miRNA targeting molecules. The application of PNAs is limited by their low cellular uptake. Currently, no simple and efficient delivery strategies are available to solve this open issue. One of the most promising approach is the modification of the PNA structure through the covalent linkage of poliarginine (R8) tails. Alternatively unmodified PNAs might be carried by nanosystems. We propose argininocalix[4]arene (1) as non-covalent vector for the delivery of anti-miR-221 PNA, which was previously demonstrated to be able to target miR-221-3p, altering its biological activity and providing a clear-cut endpoint for evaluation of its biological effects (2). The human glioma U251 cells were used as cellular model system. Our results indicate that argininocalix[4]arene 1 is a unique molecule for efficient delivery of PNAs. Most interesting features of this compound are the ease of preparation, the structural simplicity associated to high delivery efficiency and very limited toxicity. Despite uptake efficiency of PNA delivered by argininocalix[4]arene 1 is comparable with that of PNA functionalized with R8 peptide, its use results much more convenient because avoids any modification on the PNA molecules and the transfection formulation is simply attained by mixing vector and PNA. Argininocalix[4]arene 1 represent a universal vector for unmodified PNAs.

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ACKNOWLEDGEMENTS

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Caco-2 cell model for nanomaterial safety assessment: applications and future perspectives

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The evaluation of nanomaterials (NMs) ability to interact and cross biological epithelial barriers is a crucial issue in the assessment of their potential toxicological properties as well as for their risk assessment. Among these barriers, the intestinal epithelium represents one of the most relevant since it is related to oral exposure, one of the main route of entrance of NMs. The intestinal epithelial barrier model based on Caco-2 cell line represents a widely consolidated model for measuring active and passive absorption of drugs and chemicals. Recently, it has been successfully applied also to NMs fate and toxicity. Derived from a human colon carcinoma, Caco-2 cells spontaneously differentiate into enterocyte-like monolayer with many typical morphological and functional properties of the absorptive enterocytes as, for example, the development of brush border and tight junction structures. ISS has been involved in several national and European projects (i.e. NANoREG and NanoReg2) in which Caco-2 differentiated cells were used both for cytotoxicity assessment and for evaluation of barrier crossing. However, the monoculture has numerous limitations, mainly related to the greater structural complexity of the intestinal epithelium *in vivo*. The use of co-cultures with different types of intestinal cell lines, has greatly expanded the model's application capabilities. For this purpose, in the framework of a national project, ISS is setting up a triple cell co-culture model formed by Caco-2, Raji B (B lymphocytes) and HT29-MTX (mucus-secreting) cells. This model, being more closed from morphological-functional point of view to the *in vivo* situation, might represent a very useful tool to investigate NMs intestinal absorption.

This study was partially supported by the Italian Ministry of Health - chapter 4145 REACH

Physico-chemical characterization of different formulations of Nanopesticides

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Plant Protection Products (PPPs) containing nanomaterials (NMs), known as nanopesticides, are a new category of products used in agriculture to protect crops from pest and disease. The nanosize allow overcoming some problems over similar traditional ones, through a selection of physico-chemical properties.

In the framework of a national project on nanopesticides, the complete characterization of four PPPs was carried out by determination of morphology, particle size and size distribution, and composition. The formulations selected are wettable powder (WP), capsule suspension (CS), oil based suspension concentrate (OD) and emulsifiable concentrate (EC).

The Z-average (Zave) and Polydispersity Index (PDI) obtained by Dynamic Light Scattering (DLS) are in the range 27.4-148.7nm and 0.136-0.89 respectively. The root mean square radius (rms radius) measured by Field Flow Fractionation (FFF)-Multi Angle Light Scattering (MALS) ranged 39.1-82.0 nm. These values show the presence of NMs in all PPPs studied. A confirmation analysis was performed by Electronic Transmission Microscope (TEM), which provides structural and dimensional parameters of NMs. The four PPPs have NMs with size <100 nm for at least one of the three dimensions and in percentage amounts higher than 50 %.

The nanofractions, separated by FFF, are also analyzed by liquid or gas chromatographic techniques coupled with Tandem Mass Spectrometry (MS/MS) or Diode of Array Detector (DAD) in order to identify the presence of active substances. The results obtained show that the NMs are loaded with the active substances, with exception of EC formulation.

This study was supported by the General Directorate for Hygiene and Food Safety and Nutrition, Ministry of Health –Rome, Italy

Nanoengineered smart containers for induced drug release

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Controlling the drug release is one of the main goals of nanomedicine. We decided to develop polymeric nanoengineered smart containers that are able to encapsulate and release the drug in a controlled manner. These smart containers are prepared both in form of capsules and in form of arrays of freestanding microchambers.

The main technique used for the fabrication of these systems is the layer-by-layer technique that consists of the alternate adsorption of a polycation and a polyanion onto a sacrificial template, creating polyelectrolytes multilayers (PEM) capsules or chambers having the desired shape and size. Since these PEM-based systems are still permeable to small compounds, we also investigated the possibility of creating microchambers with other materials that are suitable for long-term encapsulation of small molecules (down to 1 kDa). To this aim, we used biodegradable, biocompatible, U.S. Food and Drug Administration (FDA) approved polymers to fabricate microsized drug reservoirs using one-step dip coating technique.

Experiments on the drug loading in both capsules and microchambers are also discussed. The morphology of each sample was investigated by Scanning Electron Microscopy (SEM). Furthermore, the coherent X-ray diffraction imaging technique was employed in the case of capsules to determine the influence of environment conditions on their structure. The interesting obtained results are reported. Finally, studies regarding release methods are still in progress.

Bioristor: a new sensor to increase water use efficiency in crops and trees

B.13

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The climate is changing so should we. Environmental constraints such as drought and extreme heat events strongly affects crop yields, food quality, and security. These changes claimed for new methods to monitor continuously the plant health status, to increase the efficiency of the agriculture management, to fine tuning the water supply, and to select new genetic material more adaptable to the ongoing challenges. In our research programs we developed the Bioristor, an in vivo textile-organic electrochemical transistor (OECT) sensor directly inserted into the plant stem; the sensor is able to detect changes in the ion content of the plant sap following external environmental stimuli. When integrated into tomato plants challenged with drought stress, it allowed an early detection of the stress and monitoring plant sap dynamic changes during the plant defence responses. Both genomic and environmental variables are relevant to determine water deficiency. On one side we used the bioristor to monitor a mutagenized tomato population to search for ABA-mutant with a prompt response to drought stimuli. In a second experiment we studied how the vapour pressure deficit can be handled with the use of bioristor to reduce water losses during indoor plant growth, simply monitoring the changes occurring in sap ion content due to the VPD environmental changes. Moreover, we demonstrated how bioristor can be used for water management in several food crops and trees like *Actinidia chinensis* and *Olea europaea*.

Textile wearable sensors for real-time health monitoring through sweat chemical analysis

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Monitoring of physiological parameters - in non-invasive ways - is a mandatory requirement for most “smart” wearable applications.

IMEM-CNR has developed an interesting and scalable approach¹ for the manufacturing of wearable biosensors, based on the functionalization of industrial textile fibers with conductive polymers. These devices, based on an organic electrochemical transistor (OECT) architecture, enable the continuous monitoring of the electrolyte concentration in fluids a/o complex mixtures. Textile-based OECTs have been successfully applied for detection of ionic species and biomolecules in human sweat.

To improve the selectivity of the device, different functionalization have been tested².

Firstly, the use of selective ionic membranes allows to discriminate between different cations (*e.g.* potassium and calcium); on the other hand, the use of “reactive” electrodes has been tested for the detection of specific bioactive molecules (*e.g.* glucose, lactic acid, amino acids). Finally, the development of miniaturized electronics with wireless connectivity, enables real-time collection, transmission and processing of biometric data towards remote devices (smartphone, remote server, cloud) whose provides feedback to the end-user. The availability of such biometric data are of paramount importance for monitoring the physiology and assess the well-being of patients, athletes and workers.

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Growth, characterization and chemical functionalization of germanium nanowires: building blocks for explosive gas sensors

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We report on the growth, the structural and the electrical characterization of germanium nanowires (NWs) and their chemical functionalization, proposed as building blocks for the realization of sensors tailored to explosive detection.

Germanium NWs were grown by Vapour Phase Epitaxy using isobutyl germanium, a novel Ge source as an alternative to the more commonly used germane. The optimization of the growth procedure resulted in Ge NWs up to 30 μm in length, vertically oriented on Ge (111) and Si (111) substrates.

The NWs were detached from the substrates with ultrasonication and dispersed on a carrier substrate with Au interdigitated electrodes. Single NWs were contacted to Au electrodes with Pt deposited by Focused Ion Beam (FIB). Linear I-V characteristics showed the ohmic nature of Pt-NW contacts, with electrical resistivity values in the 0.05 - 0.5 ohm cm range.

To obtain a high selectivity and sensitivity, the nanostructures were decorated with chemical moieties able to interact with the explosive molecules. In particular, the electron-poor aromatic ring of TNT is well known to strongly bind electron rich, basic and nucleophilic amino groups.

Three different synthetic strategies were followed for the functionalization of Ge NWs:

- Hydrogermylation of alkenes and alkynes on hydride-terminated Ge NWs
- Alkylation by thiolation of hydride-terminated Ge NWs
- Alkylation by Grignard reagent of halogen-terminated Ge NWs

The resulting organic functionalization was characterized by transition electron microscopy (TEM), X-ray photoelectron spectroscopy (XPS), infrared spectroscopy (ATR-FTIR) and contact angle measurements.

Synthesis of niobate based nanomaterials for piezoelectric generators

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Piezoelectric materials attract great interest due to their possible application in various fields such as energy harvesting or electronic bio-integration [1]. In the present communication, we describe a new and efficient synthesis of piezoelectric nanomaterials (niobates) and some preliminary tests about their incorporation into polyvinylidene fluoride (PVDF) polymeric film for the preparation of nanocomposites. The encapsulation in polymers improves the mechanical properties of the materials such as flexibility and stretchability. Moreover, the ferroelectric phases of PVDF contribute to enhance the piezoelectric response of the multicomponent film [2]. The piezoelectric inorganic materials with crystallinity and morphologic control have been prepared by a new microwave assisted non-hydrolytic processes. The structural properties and purity of the phases have been investigated by X-ray diffraction while the particle morphology has been analyzed with electron microscopy techniques. The multicomponent films have been investigated by scanning electron microscope to probe the heterogeneity and the thickness of the films.

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DLP 3D-printed self-healing hydrogels

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Self-healing (SH) hydrogels are smart soft materials able to autonomously recover their properties after mechanical damage without requiring the presence of an adhesive. Those materials are of increasing importance especially in scaffolds, actuators and sensors [1]. Up to now, the processing of these materials through stereolithographic additive manufacturing technologies (such as Digital Light Processing - DLP) has been challenging because of their opposite requirements in terms of cross-linking density [2]. It would be of great impact to build complex 3D structures with SH hydrogels for their application in biology and underwater environments. In this work, we overcame the incompatibility between 3D printing and self-repairing properties by using an interpenetrated double network, made of chemically cross-linked Acrylic Acid (AAc) and an electrostatically cross-linked Polyvinyl Alcohol (PVA). We propose the use of PVA as mending agent, that provides self-healing behavior thanks to its strong hydrogen bonding [3]. A waterborne formulation, containing a PVA solution, AAc, and a water-soluble photoinitiator, was used to print complex soft samples using a commercial DLP system. Healed samples showed a 72% recovery in mechanical strength, which increased to 91% with the addition of Polyethylene Glycol (PEG) in the formulation. The proposed solution opens the way for new relevant applications of 3D printing such as mendable soft robotics.

Figure 1: Cylindrical sample (a) as printed (b) cut (c) rejoined (d) stretched after 8 h healing (reference bar 4 mm).



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DLP-3D printing of functional materials

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3D printing technology has recently grown showing great potentialities that make it suitable for a variety of application fields: from biomedicine to electronics and even further.

The development of new and advanced materials suitable for the different existing techniques plays a fundamental role in this revolution.

The research presented is focused on materials for printing technologies based on solidification upon exposure to a light source, and, in particular, for digital light processing (DLP). The final properties of the printed objects can be tailored by simply changing or charging the reactive liquid formulations, playing with the precursors used a large variety of systems can be conceived for the production of structures with advanced properties and suitable for further functionalization steps.

Three-Dimensional Printed Photoluminescent Polymeric Waveguides

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In this work, we propose an innovative strategy for obtaining 3D printed polymer waveguides and splitters employing a light activated additive manufacturing technology, specifically Digital Light Processing (DLP). This technology is based on the spatially-controlled solidification of liquid formulations through fast photopolymerization reaction [1]. Typically, the materials processed by DLP present 3 main ingredients: monomers, photoinitiator and a dye. While the first one will constitute the printed object and the second controls the reactivity towards the light and so the printing rate, the third one is added at low concentrations to control the light penetration, allowing to obtain well-defined structures. However, after the printing process is usually useless, giving a residual colour, often undesired. [2]

Here [3] we exploit the necessary use of the dye for producing 3D printed waveguides and splitters able to guide luminescent by using a photoluminescent dye specifically synthesized for this purpose without affecting the printability of the formulation.

Moreover, by copolymerizing the dye with the polymeric network during the printing process, it was possible to transfer the solvatochromic properties of the dye towards different solvents to the printed structures, enabling the development of solvents' polarity sensors.

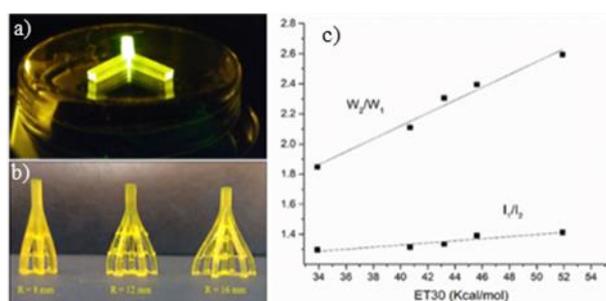


Fig. 1. a) Fluorescence pictures of the 3D printed waveguides illuminated at one end of the device. b) complex-shaped 3D printed waveguides. c) Variation of fluorescence emission band of the 3D printed structures by swelling in different solvents represented as the ratio of the intensities (I_1/I_2) and the full widths at half-maximum height (W_2/W_1). Subscripts 1 and 2 refer to peaks assigned to individual NBD molecules and aggregates, respectively.

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Laser-induced 2D nanostructured materials for energy storage into supercapacitors

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Graphene and graphene-like materials have been intensively studied in the field of electrochemical energy storage, and in the last three years the research focus has been broaden on new layered 2D-materials, such as MoS₂ and other transition metal dichalcogenides. Recently, laser-induced graphene (LIG) has been proposed as an efficient active material for flexible supercapacitor (SC) electrodes. This material consists of a 3D network of multilayer graphene obtained by a laser writing process on polymer surface during which the sp³-carbon atoms in the polymer are photothermally converted to sp²-carbon atoms. Herein we are reporting a rapid one-pot synthesis of MoS₂-decorated laser induced graphene by direct writing of polymeric foils. By covering the polymer surface with a layer of MoS₂ dispersion before processing, it is possible to obtain an in-situ decoration of porous graphene network during laser writing, enabling both electric double layer and pseudo-capacitance behavior (Figure1).[1] Additionally, a simple method to transfer the LIG porous layer obtained onto polyimide sheet to a transparent and elastomeric substrate (PDMS) is proposed. [2] The elastomeric nature of the host matrix allows high deformation-tolerance of the fabricated devices that demonstrate great potential for the development of stretchable and wearable energy storage sources.

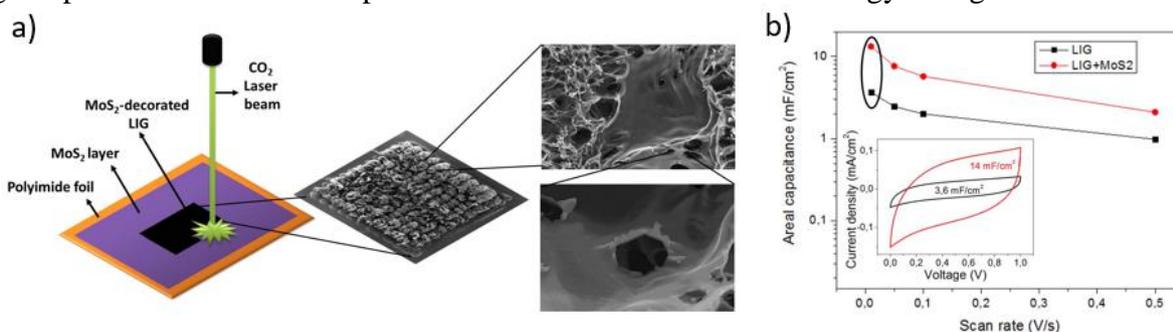


Figure 1. Scheme of the fabrication process of the laser-induced graphene decorated by MoS₂ flakes together with electron microscope images (a) and its electrochemical performances in aqueous based electrolyte (b).

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Study of the stability of textile bioelectronic sensor in smart devices

B.21

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During these years the development of “smart” devices has seen a high degree of integration in everyday products thanks to their ability to collect and exchange data in real time. The development of integrated sensors is important to collect data continuously for the analysis of the environmental sample. In the specific, organic electrochemical transistors, OECTs, are biosensors with a transistor structure, able to monitor ionic concentration in an electrolytic solution. The application of conductive polymer PEDOT: PSS, to functionalize textile threads, allowed to obtain a wearable and biocompatible integrated biosensor. Thanks to this approach, this biosensor is used in many devices and applications: to monitor the plant physiology, by directly integrating the biosensor in the plant stem, or to monitor the human sweat characteristic, by embedding the device in a sport T-shirt. Among the different characteristics of a biosensor the response stability could be crucial for specific applications. Here we considered two different methods for the sensor preparation: i) by adding ethylene glycol as solvent or ii) by performing a post treatment with pure sulfuric acid. The sensor response was tested for several weeks. The primary sensor degradation mechanism was found to be gate degradation due to physical detachment of the PEDOT: PSS from the electrode in presence of higher gate voltages. The reduction of gate voltage allowed to increase sensor lifetime for the desired operating conditions. Moreover, the sulfuric acid treatment allowed to obtain more stable sensors.

Study of Ni decorated Graphene based electrodes for Asymmetric Supercapacitors

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The current energetic demand requires new devices capable of storing and returning large amount of energy with high speed and efficiency. Large scale use of batteries still suffers from conversion efficiency, high cost, limited life-time and disposal problems.

In this context, supercapacitors (SCs) are receiving widespread attention, thanks to their higher specific power, greater efficiency (95%) and a much longer average life than batteries. However, their specific energy is still at least one order of magnitude less than in batteries, thus limiting the applications for such devices. Nevertheless, the specific energy can be increased by coupling the SC physical capacitance with a “pseudo-capacitance”, and/or by extending the electrochemical working window of devices, for example making asymmetric SCs.

Here we present a novel asymmetric SC made with graphene as anode, and graphene decorated with nickel nanoparticles (Ni-NPs) as cathode, operating with an aqueous electrolyte (KOH 3.5M). Our peculiar graphene, obtained by thermal exfoliation of graphite oxide, is particularly suitable for anchoring metal nanoparticles, due to the large amount of active defects produced during the synthesis process.

The electrodes were characterized by means of powder X-Ray Diffractions, SQUID magnetometry, X-Ray Photoemission Spectroscopy and three-electrode cyclic voltammetry. We proved that, during the charge/discharge process, the Ni-NPs transform into Ni(OH)₂ and participate in battery-like redox reactions, thus extending the specific capacitance.

The final device, characterized by two-electrode cyclic voltammetry, galvanostatic charge/discharge cycles and impedance spectroscopy, displayed also an extended electrochemical working window, which further allowed increase its energy density.

Stimuli-responsive thiol-epoxy networks with photo-switchable bulk and surface properties

B.23

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In the present work, the versatile nature of o-nitrobenzyl chemistry is used to alter bulk and surface properties of thiol-epoxy click networks. By introducing this irreversible photocleavable chromophore into polymer networks, the material properties can be switched locally by light of a defined wavelength. In this work the synthesis of photo-responsive thiol-epoxy network follows a base-catalyzed nucleophilic ring opening of epoxy monomers with photolabile o-nitrobenzyl ester (o-NBE) groups with multi-functional thiols. To ensure a temporal control of the curing reaction, a photolabile base is employed as catalyst, which is activated by both UV-light and temperature. The spectral sensitivity of the photo-latent base is extended to the visible light region by adding a selected photosensitizer to the resin formulation. Sol-gel analysis evidences the formation of soluble species, which is exploited to inscribe positive tone micropatterns within the thiol-epoxy networks. In particular, patterns with a structure size of 50 μm are realized by photolithographic techniques. Along with the localized tuning of network structure, the irreversible photoreaction is exploited to change the surface wettability of thiol-epoxy network. The contact angle of water significantly decreases upon UV exposure due to the photo-induced formation of hydrophilic cleavage products. Thus, the thiol-epoxy networks do not only provide a fast cure- and cleavage-on-demand after light exposure at different wavelengths but also a convenient approach to tailor surface characteristics.

Energy harvesting and storage system for indoor application

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On the path towards independence from fossil fuels, solar energy is the most promising solution, but it needs a robust and reliable storage system to face its intrinsic fluctuations due to location, day cycle and weather. The integration between harvesting and storage technologies is a must toward clean energy production and it becomes even more appealing considering the possibility of producing electricity not only from direct sunlight but also from diffuse light and indoor illumination.

Dye-sensitized solar cells (DSSC) showed an impressive light-to-energy conversion efficiency when employed under low-light illumination, diffuse solar radiation and indoor light sources. Moreover, low temperature- and atmospheric-pressure-based manufacturing processes make them compatible with roll-to-roll fabrication. This make DSSC an engaging alternative in the landscape of recovering energy from indoor illumination and directly power low-consuming devices (e.g. Internet of Things devices).

For the storage section, electrochemical double layer capacitors (EDLCs) represents a promising solution since they can sustain an incredible number of cycles without appreciably change the capacitance nominal value and they are less sensitive to the voltage output of the harvesting section like a battery. These features perfectly match with the intermittent character of photovoltaic energy production.

Herein we present a DSSC module developed to harvest indoor illumination and directly store it into an EDLC. Six series-connected DSSC are fabricated on the same substrate and the module is integrated with a high-voltage EDLC. The integrated device is characterized under indoor light sources (e.g. LED, fluorescent, halogen lamp) and under mixed natural and artificial light illumination.

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Development of layer-by-layer assembled MWCNT transparent thin film electrode

B.25

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Transparent electrodes are indispensable components in every optoelectronic device. There is a need for development of new thin film electrodes that will have high transparency in mid-IR range. Transparent electrodes were developed from multi-walled carbon nanotubes (MWCNT) and polyelectrolyte by layer-by-layer (LbL) assembly. LbL is a unique technique for deposition of the ultra-thin films with the ability to control the thickness. The technique consists of alternate deposition of positively and negatively charged amphiphiles on the substrate. In that sense, polyethylene imine (PEI) and carboxylic MWCNTs (MWCNT-COOH) were deposited alternately on the glass substrates. Samples were prepared with different number of bilayers (PEI + MWCNT-COOH) and the thickness of the films varied between 100 and 300 nm, depending on the number of bilayers. After the deposition of each layer, samples were thoroughly washed with DI water to remove excess material and dried at 120 °C for 10 min after each bilayer deposition. MWCNTs and fabricated thin film electrodes were characterized with Raman spectroscopy, high-resolution scanning and transmission electron microscopy. Relative sheet resistance of developed electrodes was measured with four-point probe station and the values were ranging from 4 kΩ/sq up to 10 kΩ/sq, depending on the number of layers. Transparency of samples was measured in mid-IR range. Samples had transparency between 50 and 70% at 3000 nm.

Efficient SERS-active platforms obtained from different fabrication routes

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Surface-enhanced Raman scattering (SERS) spectroscopy is an extremely powerful analysis technique that has attracted a lot of interest in several application fields, ranging from analytical chemistry to biomedicine, since it allows the non-invasive, label-free detection of chemical and biological specimens with high sensitivity, even down to the single molecule scale.¹ SERS technique relies in the detection of analytes Raman scattering signals, amplified by electromagnetic fields produced by the optical excitation of localized surface plasmon resonances of nanostructured metal substrates. The strength of the SERS signal is directly dependent on the nanopattern geometry. In particular, strong SERS signal enhancements, i.e. hot spots, were observed at junction between adjacent nanostructures² and at sharp edges of anisotropic nanostructures.³ The major challenge resides in the achievement of SERS substrates with superior signal amplification together with high uniformity and reproducibility. Furthermore, in view of the development of SERS-based integrated sensing/imaging systems for advanced biomedical applications, the fabrication processes should be compatible with unconventional substrates, like optical fibers tips.⁴ Here we present different approaches for the development of highly efficient SERS platforms, based on both electrochemical and self-assembly techniques. We highlight the relation between the fabrication process conditions and the morphological features obtained through a combination of scanning electron microscopy and atomic force microscopy images. Furthermore, we characterize the SERS response of standard analytes deposited on the different platforms and we demonstrate that the fabrication strategies adopted can be exploited for the development of SERS-active optical fibers.

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Responsible development of remotely controlled enzyme-nanoparticle systems (NANOZYMES)

C.01

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We have recently shown that the catalytic activity of enzyme-nanoparticle systems can be remotely controlled by alternate magnetic fields ^[1]. From this observation, it originates the interdisciplinary FET-OPEN project HOTZYMES that envisions remote and tunable nanoactuation of single as well as multi-enzymatic processes (<https://www.hotzymes.eu>). Indeed, one-pot multi-enzymatic systems are an efficient alternative to chemical synthesis for the production of high-value chemicals. We think, however, that the remote control of enzymatic activity is not exploitable only in industrial biocatalysis, but also in nanomedicine to intervene in the cellular metabolism.

In the frame of this project, we are producing several new metal-based nanoparticles with a large spectrum of magnetic characteristics and surface functionalizations for enzyme binding optimization. Therefore, it behooves us to evaluate their safety. To this aim, after performing conventional toxicity tests of nanoparticles that are synthesized for our project, we started to analyze their possible epigenetic toxicity. There are, indeed, increasing evidences on the heritability of nanoparticle mediated toxicity that could be explained by epigenetic modifications ^[2].

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Mechanical properties of Chronic Lymphocytic Leukaemia cells

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Chronic lymphocytic leukaemia (CLL) is one of the most common and incurable B cell leukaemia. CLL cells traffic between peripheral blood, bone marrow and secondary lymphatic tissues where interact with a supportive microenvironment. These processes are affected by the mechanical forces present in the environment and by the capability of the cells to sense the forces. In order to migrate from a fluid environment like the blood to a significantly more viscous surrounding, B lymphocytes need to modify their cytoskeleton and consequently their rigidity. Those processes are known to be regulated by Hematopoietic-cell-specific Lyn-substrate-1 (HS1) protein, which promotes the homing processes and is involved in cell-cell communication and focal adhesions formation.

From a nanomechanical point of view, cytoskeleton rearrangements can be observed as a difference in the force distribution along the cell and, ultimately, as a change of the overall rigidity of the cell. To measure this change, we used Atomic Force Microscopy (AFM) in Force Spectroscopy Mode (FSM) as an external pressure stimulus and we observed the cell deformation, which finally determines the value of its stiffness. By AFM we measured primary B lymphocytes from selected CLL patients and healthy donors, and we found a significant decrease of stiffness in leukaemia cells compared to healthy ones. Then we tested the effect of a first line drug (Ibrutinib) on the mechanical properties of both leukemic and healthy cells.

We are planning to extend our analysis to investigate the contribution of the microenvironment that leukemic cells exploit during their settlement and growth of the tumor.

Understanding nanoplastics through the nanomaterials analysis

C.03

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Plastic pollution is a great issue affecting our Planet, especially marine ecosystems. Once enter the environment, plastics undergo degradation processes and fragment into smaller pieces up to the nanoscale.

Damages caused by large plastic items to marine organisms are well known; microplastics pollution of oceans and seas has been investigated in depth too, and several studies have demonstrated the presence of microplastics (size less than 5mm) in the gastrointestinal tract of fishes and marine mammals.

Recently, another group of plastic debris, called nanoplastics (size less than 1000nm), has gained more attention. Unfortunately, the small size of these pollutants makes their isolation from the environment difficult, and this fact also strongly hampers their characterization. In addition, nanoplastics are not nanomaterials synthesized with the desired size, shape, surface, and composition. As a consequence, another issue is how to produce nanoplastics at the laboratory scale, in a way that mimics what happens in nature. Create a good reference material may allow scientists to better understand the characteristics of nanoplastics and how nanoplastics interact with marine environment and living ecosystem.

In this work, we present a preliminary study on the production, isolation and characterization of nanoplastics. Starting from commonly used disposable plastic items, we used mechanical disruption to fragment macro-pieces into nanoplastics in a controlled way. Combining filtration and centrifugation processes, we were able to concentrate nanoplastics. Finally, we used consolidated techniques in the field of nanomaterials, such as scanning probe microscopy, size distribution and physical-chemical characterization techniques, to provide a fingerprint of nanoplastics.

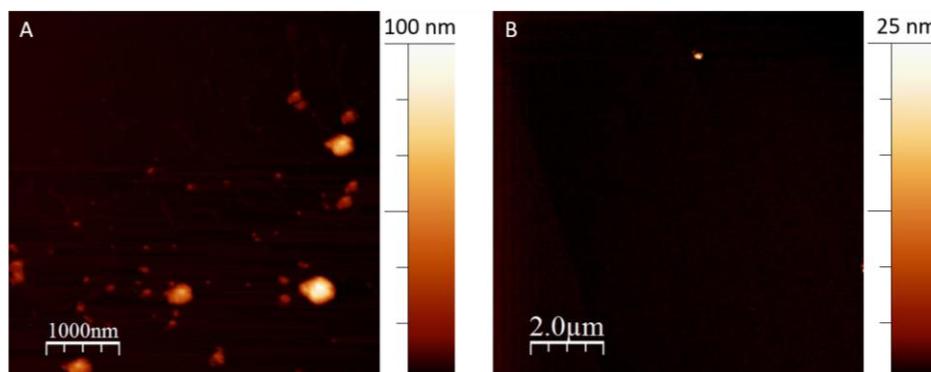


Figure 1.

AFM images:
PS nanoplastics (A);
control water (B).

Nanoparticles modify embryonic genes expression in *Xenopus laevis*

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Nanoparticles (NPs) exposure is inevitable as they are increasingly used in different areas. In medicine they assist the diagnosis of diseases. Their versatility is used for drug delivery system. The food industry also widely uses nanotechnology. NPs can penetrate into cells and interfere with their activity. They can also accumulate in organisms and in the food chain. Despite the rapid development of nanotechnology, informations on the exposure of organisms and environment to NPs is still limited and its implications have not been sufficiently explained. Therefore it is important to assess the risks associated with nanotechnology in order to identify potential damage. Exposure of organisms to the nanoparticulate is potentially hazardous, particularly when it occur during embryogenesis. Here we studied the effects of some nanoparticles (AgNPs, AuNPs, SiO₂NPs; MKnano, Canada) on the embryogenesis of *Xenopus laevis*, a model for these kind of studies. The possibility of relating the data obtained in *Xenopus* with higher vertebrates, including humans, makes it a convincing study model. These NPs have been used to understand the possible consequences of similar NPs utilized in medicine or food. The embryos were reared from st. 2/4 in FETAX containing 0.01, 1 and 5 mg/L of NPs and harvested at stage 46/48. As control, sibling embryos were used. Our data show that all NPs aggregate into FETAX (DLS data) and do not cause mortality but affect embryonic development. To explain the origin of the embryonic problems we verify the ROS production and the expression of some genes involved in early embryogenesis (fgf8, bmp4, sox9, pax6, egr2, rax1). We have shown that these NPs stimulate increased of ROS production and changes in gene expression depending on the NPs concentration.

Synergistic activity of polyaminocyclodextrin-silver nanocomposites with ampicillin and apramycin antibiotics.

C.05

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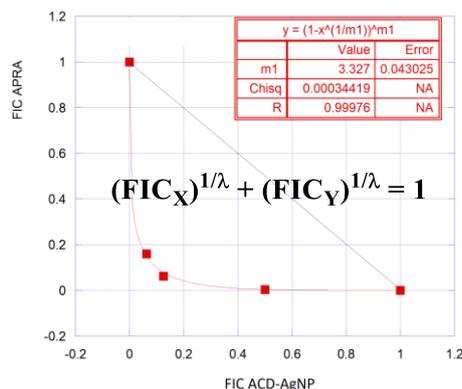
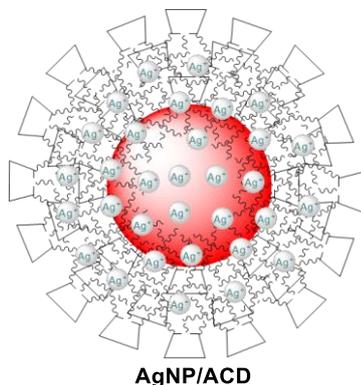
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The selection and spread of antibiotic-resistance pathogenic bacteria has undermined our capability to prevent and treat infectious diseases. Composite systems constituted by silver nanoparticles (AgNPs) stabilized by polyaminocyclodextrins (ACD)¹ can be conveniently synthesized by a photoreduction protocol, avoiding the use of non-bio-friendly reactants. The nanocomposite AgNP-ACD systems, which were fully characterized by a physico-chemical point of view, were considered as potential platforms for developing innovative strategies to face up with the problem of antimicrobial resistances¹.

The combined effect of AgNP-ACD systems with either ampicillin (AMP) or apramycin (APRA) antibiotics was investigated by evaluating the growth inhibition of various bacterial tester strains (*Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Kocuria rhizophila* and *Staphylococcus aureus*). The results were expressed as the ratio between the inhibitory concentration of a given biocidal in combination with the other one and the minimum inhibitory concentration (MIC) of the same biocidal alone (FIC values). These values were then analyzed in term of isobolograms and rationalized by means of the Syberg equation.² Both antibiotics showed a significant synergistic effect (quantified by the λ coefficient in Syberg equation) with the AgNP-ACD composite. Studies on the possible physico-chemical interaction between the antibiotics and the composite, as well as on the possible biological mechanisms implied in synergism, are currently in progress.

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Sub-micropillar spacing modulates the spatial arrangement of osteoblasts

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In the last few years it became evident the importance not only of the micro-, but also the nano-topographical organization of extracellular signals, in order to control cell adhesion, proliferation and differentiation to regenerate the tissue and improve the clinical performances of dental implants. The nanoscale surface morphology provides an increased implant-surface area that can react with the microenvironment, thus considerably influencing cellular response.

In the present study we developed two spatially defined silicon surfaces with nanopillars arranged as hexagons and we observed the behavior of murine osteoblasts. In particular, cell adhesion and proliferation were studied through immunofluorescence for focal adhesions and chemiluminescence assay, respectively. Moreover, a morphological analysis of cells was carried out with SEM/FIB microscope and their perimeter, area and elongation factor were quantified and analysed with a Br5.11 software (Nikon).

As it appears clear from the images, cells attached and proliferated well on the nanopatterns, trying to follow specifically the shortest inter-pillar distance, thus creating consistent morphological modules. A particular extracellular protein secretion has been seen to preced and envelop the cell, or more in detail, its cytoplasmic orientation, underlying the close integration of surface nanopatterning with extracellular protein deposition and cell arrangement. Focal adhesion analysis confirmed the tight relationship between cell shape and pillars disposition.

The development of a material with well-organized nanostructured pattern becomes fundamental control and direct cell spatial order and cell behavior, to maximize osteoblastic maturation and bone deposition for biomedical applications such as implant dentistry.

Antimicrobial potency of Ag-chitosan nanocomposites against clinically relevant bacteria *Escherichia coli* and *Staphylococcus aureus*

C.07

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Health-care associated infections and the increasing development of antimicrobial resistance to the conventional antibiotics are among the most serious public health problem globally. Nanotechnologies open new possibilities for the creation of efficient and safe antimicrobials for the biomedical application, e.g., wound-dressing materials that enables to reduce/avoid microbial infections and the formation of antibiotic-resistant strains.

We aimed to (i) synthesize Ag-chitosan-nanocomposites (Ag-CS-NCs) and (ii) evaluate their antimicrobial potency towards medically relevant bacteria Gram (-) *Escherichia coli* and Gram (+) *Staphylococcus aureus*.

Ag-CS-NCs were synthesized by the reduction of AgNO₃ with NaBH₄ in the presence of chitosan. Two differently sized Ag-CS-NCs were synthesized: ~200 nm (Ag-CS₂₀₀) and ~400 nm (Ag-CS₄₀₀) (hydrodynamic size, d_H). ζ -potential of Ag-CS-NCs was +28 and +37 mV, respectively. Antimicrobial potency of Ag-CS-NCs was addressed by determining their minimum biocidal concentration (MBC) in deionized (DI) water to minimize the influence of silver ions speciation on its bioavailability and toxicity. In parallel, AgNO₃ was analyzed as an ionic control.

We showed that studied Ag-CS-NCs were efficient antimicrobials towards bacteria *E. coli* and *S. aureus*: 24-h MBC values ranged from 0.08 – 0.16 mg Ag/L and 0.23 – 0.31 mg Ag/L, respectively. Both studied Ag-CS-NCs were more potent to *E. coli* than to *S. aureus* and Ag-CS₂₀₀ (d_H ~200 nm) were more potent than Ag-CS₄₀₀ (d_H ~400 nm) to the both bacteria.

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Circular nanochemistry for Nitrogen-Doped Carbon Dots as promising material for biobased applications

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In the last 10 years the interest on carbon dots (CDs) has been progressively increased in different fields. Their remarkable advantages in terms of low toxicity, chemical inertness, tunable fluorescence, good water solubility, and physicochemical properties make them suitable for bio-based applications and in particular in the biomedical field [1], [2]. Another peculiarity of CDs is that their synthesis fully responds to the principles of the circular chemistry.

In the present work, we show the synthesis, characterization and preliminary applications of nitrogen-doped CDs (N-CDots). N-CDots were synthesized by one-step hydrothermal methods starting from waste/renewable materials as citric acid and urea. TEM, XRD and FT-IR analysis confirmed the nature of the N-CDots. UV-Vis absorption and photoluminescence spectra showed that optical properties of N-CDots can be tuned over the visible spectrum by simple modifications of synthetic conditions.

Particularly, N-CDots with absorption above 470 nm were selected to evaluate their cytotoxicity and internalization at 24 and 72h. On the basis of the obtained results their photocatalytic activity will be tested with the aim to modulate the generation of reactive oxygen species (ROS) in the cell cytosol. Moreover, blue/green emitting CDs were used as secondary carbon source for the microbial fermentation of *Gluconacetobacter xylinum* and bio-based fluorescent bacterial cellulose hydrogels were obtained.

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Bioprintable hybrid ECM for cell modelling and bioengineering applications

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Tissue engineering is an inter- and multidisciplinary field that combines the principles and technologies from engineering, material science, chemistry, cell biology. Aim of the field is to develop functional substitutes able to restore and substitute injured or damaged tissues.

New technologies are available to produce functional tissues. In particular, by 3D printing and bioprinting today is possible to control both composition and architecture of the final construct. The major challenge of this approach is to print three-dimensional supports preserving cell viability and functionality as well as ensuring the structural integrity of the scaffold. To overcome this challenge, new bioresponsive polymers are needed. With this aim, mimetics of natural ECM components were designed and produced to investigate the influence of polymers properties and different formulation processes. Cell viability and functionalities were also investigated to assess the bioprinting processes and to produce tissue scaffolds with embedded living cells.

In particular, natural polymers such as chitosan and gelatin are promising biomaterials for the preparation of biodegradable hydrogels due to their excellent biocompatibility and biological functions. In this work we propose the development and the assessment of new smart hybrid biomaterials in three different formulations: fibrous scaffold, injectable hydrogel and bioprintable hydrogel.

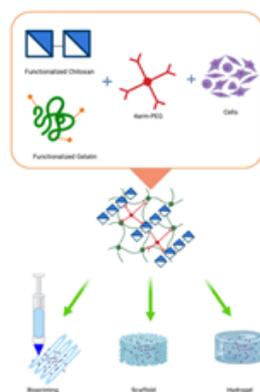


Figure 1: Schematic illustration from biomaterials to bioprinting, scaffold and hydrogel formulation.

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AFM Single-Molecule Force Spectroscopy of α -Synuclein Structures

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Protein misfolding and toxic aggregation are very critical steps in the development of several neurodegenerative diseases, including Parkinson's disease, induced by the fibrillation of the intrinsically disordered protein α -synuclein. Thus, elucidating properties of α -synuclein in misfolded states and understanding the mechanisms that drive its assembly into the disease prone aggregates are critical for the development of rational approaches to prevent protein misfolding mediated pathologies.

Although α -synuclein lacks a single well-defined structure under physiological conditions, it was found to assume three distinct conformational states ranging from a random coil to a highly structured conformation.

Here we afford this issue taking advantage of single molecule force spectroscopy: by using the AFM we stretch and unfold a polyprotein containing the human α -synuclein. The analysis of the different state of unfolding gives information about the structural conformation of the protein before the mechanical denaturation.

Since it has been demonstrated that different ligands and inhibitors, such as Epigallocatechin-gallate (EGCG) and Dopamine (DA), have a crucial role in the fibrillation process of this protein, we performed single molecule force spectroscopy studies in the presence of EGCG or DA to investigate how these ligands could affect the 3D structure of the α -synuclein protein.

Nanoparticles Based on Sugars and Alkali-Earth Halogenides with Second Harmonic Generation properties for applications as bio-sensors and for Radiotherapy

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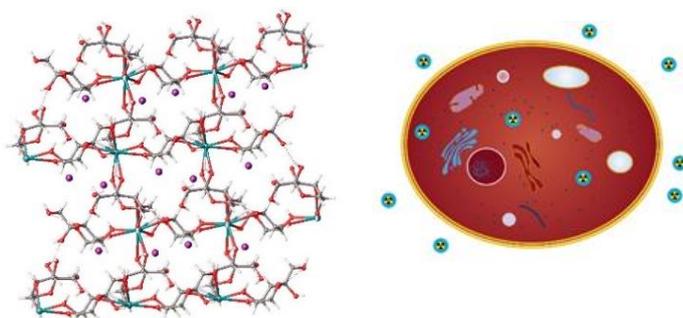
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In recent years, some Metal Organic Frameworks (MOFs) with Second Harmonic Generation (SHG) properties, based on fructose and alkali-earth halogenides, were investigated to understand the effect of cation size and anion polarizability on crucial quantities correlated to the non-linear optical (NLO) response, such as hyperpolarizability and optical susceptibility [1,2,3]. The compounds studied are interesting for biomedicine applications, as they combine high biocompatibility, due to their non-toxic components, and significant SH emission, that can permit exploitation for *in vitro* bio-imaging.

Right now, a possible application in radiotherapy is under investigation. To these purposes we synthesized nanoparticles of some MOFs, based on fructose and SrX₂ salts (X=Cl, I). The compounds were characterized by single-crystal and powder XRD, IR and RAMAN spectroscopy and the second-order susceptibility were estimated from theoretical calculations, both in vacuo and in the solid state. Furthermore, we attempted to assess the reduction of the SH intensity for small quantities of nano-crystals, in order to ascertain the possibility of applications in biological systems.

The nanoparticles were encapsulated in a phospholipidic shell and characterized by Dynamic light scattering technique (DLS). Preliminary viability assay and cell uptake tests were performed on non-tumor and tumor cell lines, hTERT-HME1 and HT-29, respectively. Furthermore, a simple computational tool to evaluate the specific activity of NPs containing ⁸⁹Sr and ¹³¹I required to deliver a pre-determined dose to the cancer tissue was developed, in order to rapidly estimate the amount of NPs to be administered to the patient. The results are discussed in the context of developing novel biocompatible materials for personalized radionuclide therapy.



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Depicting Conformational Ensembles of α -Synuclein by Single Molecule Force Spectroscopy and Native Mass Spectroscopy

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Description of heterogeneous molecular ensembles, such as intrinsically disordered proteins (IDPs), represents a challenge in structural biology and an urgent question posed by biochemistry to interpret many physiologically important, regulatory mechanisms. Single-molecule techniques can provide a unique contribution to this field.

Here is presented a work in which single molecule force spectroscopy is applied to probe conformational properties of α -synuclein in solution and its conformational changes induced by ligand binding. Our goal is to compare data from such an approach with those obtained by native mass spectrometry. These two orthogonal, biophysical methods are found to deliver a complex picture, in which monomeric α -synuclein in solution spontaneously populates compact and partially compacted states, which are differently stabilized by binding to aggregation inhibitors, such as dopamine (DA) and epigallocatechin-3-gallate (EGCG). Analyses by circular dichroism and Fourier-transform infrared spectroscopy show that these transitions do not involve formation of secondary structure.

This comparative analysis provides support to structural interpretation of charge-state distributions obtained by native mass spectrometry and helps, in turn, defining the conformational components detected by single molecule force spectroscopy.

Biodegradable nanoneedles for delivery of nucleic acids into the cornea

C.13

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The innermost corneal layer, corneal endothelium, is crucial for maintaining corneal transparency and its dysfunction is the main indication for corneal transplantation. Overcoming this invasive procedure has revealed challenging, in particular due to the limited proliferation capacity of its corneal endothelial cells (CEnC). However, CEnC growth can be induced by reprogramming of genes involved in crucial intracellular pathways, like cell cycle regulators, using a transient gene therapy approach.

Biocompatible and biodegradable silica nanoneedles (nN) have been recently shown their ability to deliver nucleic acids directly into the cells cytoplasm, with an efficiency greater than 90% and minimal toxicity.

We exploited here the delivery capacity of silica nN to transfer nucleic acids into human corneal endothelium. Silica nN chip were applied to an *ex vivo* human corneal model to deliver fluorescently labelled siRNA. CEnC showed an efficient cytoplasmic intake of siRNA, at 24 and 48 hours. Moreover, corneal endothelial cells did not show any sign of cell death following nN application. This approach represents an innovative method to deliver nucleic acid into corneal tissues, developing safe and localized gene therapy strategies.

Nanoparticles characterisation with spICP-QQQ

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In daily-use products, nanoparticles (NPs) application has experienced a rapid growth. The inorganic nanomaterials more wide spread are TiO₂, ZnO, SiO₂, Ag and other less know like FeO_x and CeO_x. Nano TiO₂, ZnO and Ag are utilized mainly in cosmetics and paints, whereas nano SiO₂ is useful in biomedical applications.

Measurement of nanoparticles (NPs) is necessary to assess their impact on food safety, human health and environmental systems.

If Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) are useful techniques to determine the size distribution, ensure size range, evidence of aggregates and obviously determine NPs shape. These methods are not able to quantify the concentration of size-dependent metal species in samples. An analytical approach for this kind of determination, with effective interference removal, in products is the Triple Quadrupole Inductively Coupled Plasma-Mass Spectrometry (ICP-QQQ), an important tool to complete sample characterization. This technique can be used as a direct technique, namely the Single Particle (SP) ICP-QQQ, that uses a direct aspiration of the sample, where each individual NP passes through the ICP and it is atomized, ionized and identified by the detector, using time resolved analysis (TRA), assuming that one peak is one NP. This application, associated to high selectivity, high sensitivity and low detection limits of the instrument, allows measuring the concentration, diameter, composition and size distribution for NPs.

We applied spICP-QQQ and SEM-EDS to characterize shape, distribution, quality, dimension and concentration of different NPs in some food supplements.

Nanoscale-specific effect of CdS quantum dots on human cells as measured by miRNA profiling

C.15

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Cadmium (Cd) ions are known to be toxic to humans and to human cells grown in vitro. Here, the consequences of exposing both hepatocellular carcinoma cells (HepG2) and macrophages (THP-1) to Cd-containing quantum dots (QDs) were compared to those induced by exposure to CdSO₄. We showed that CdS QDs and Cd ions cause different effects in the two cell lines as measured by cell integrity, Cd accumulation, mitochondrial function and the microRNome profile. The two cell types responded differently, being responsive to both dose and Cd type. While mitochondrial functionality was reduced by the presence of the CdS QDs, exposure to CdSO₄ was more damaging. Biochemical and physiological end-points found a confirmation at the level of miRNAs regulation with significant quantitative differences for QDs and Cd. Cd exposure as QDs can drive cells to apoptosis (HepG2) or to autophagy (THP-1). Moreover, Cd reduced tumor suppression potential; this important effect also differed on the basis of cell type and Cd type.

C.16

Multi-functionalized polymeric nanoparticles for pancreatic β -cells detection: developing novel multimodal *in vivo* imaging strategies

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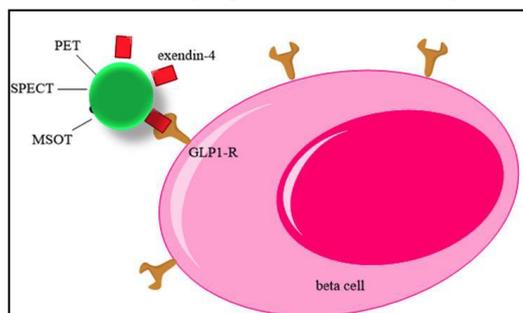
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In vivo imaging is a rapid, intuitive and non-invasive approach that can be useful for the early detection of severe pathologies, for the follow-up of patients, to display the recovery of damaged tissues as well as the therapy efficacy. Interestingly, *in vivo* imaging can become a more important tool in these fields because of the improvements in the molecular-imaging technologies. However, it needs probes in order to study physio-pathological structures and/or processes at biological and molecular level. Nanoparticles have been largely used for this aim, thanks to their very small dimensions and high surface area to volume ratio. Such large area is available to be labeled and it makes them appealing for improving the resolution of *in vivo* imaging.

Polymeric nanoparticles based on poly-glutamic acid and chitosan were prepared through ionotropic gelation. Both the polymers were functionalized with different functional groups suitable for chemo-selective ligations allowing the nanoparticles decoration with ligands for cell targeting and a couple of detecting agents. Through click chemistry reactions, nanoparticles were easily functionalized with a chelating agent for gallium or gadolinium, dodecane tetra-acetic acid (DOTA), allowing them to be detectable by SPECT (Single Photon Emission Computed Tomography), PET (Positron Emission Tomography) or MRI (Magnetic Resonance Imaging) imaging approaches. Furthermore, the nanoparticles were functionalized with IRDye800 CW, a near infrared dye viewable with MSOT (Multi-spectral optoacoustic tomography) technique. For cell targeting, nanoparticle formulation was functionalized with the peptide exendin 4, a specific ligand of the pancreatic β -cells receptor glucagon-like peptide-1 receptor (GLP-1R).



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Sialidase NEU3 is shuttled on the surface of biogenic small nanoparticles

C.17

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Sialidases (EC 3.2.1.18) are enzymes that remove terminal sialic acid residues from glycoconjugates (i.e. oligosaccharides, glycolipids and glycoproteins). The plasma membrane-associated sialidase NEU3 is involved in the fine tuning of sialic acid exposed on the cell surface. The enzyme takes part in cell communication, cell interaction with extracellular matrix and signal transduction. In our previous study, we analyzed the presence of NEU3 in biogenic nanoparticles defined as extracellular vesicles (EVs) (30 nm-1000 nm), produced by HeLa cells. Dot blot analysis revealed that NEU3 is associated with small EVs (sEVs) (30 nm- 300 nm) and localizes on the external leaflet of these nanovesicles.

NEU3 is highly expressed in colorectal cancer (CRC), in which EVs play a pivotal role in promoting cell proliferation and invasiveness. Thus, we are now investigating the topology and the activity of endogenous NEU3 on EVs released by human epithelial colorectal adenocarcinoma cell line (Caco-2). The activity of NEU3 on the EV surface is assumed to modify EV sialic acid content with possible relevant outcome on EV glycocalyx net charge and steric hindrance, influencing their biological behavior in the extracellular environment. Overall, NEU3 could be regarded as a useful marker for EV study in physio-pathological conditions. Finally, the enzyme might represent a molecular tool for shaping sEVs as possible drug carriers in personalized therapeutic approaches.

CdS QDs affect gametogenesis in *Saccharomyces cerevisiae*

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Nanotechnology is a rapidly growing field having potential applications in many areas. Engineered nanoparticles (NPs) have been widely used in several fields from medical to electronics and possess unique chemico-physical properties as compared to their bulk counterparts. The increasing interest for these advanced materials has led to great excitement about their potential benefits, but little is known about the biological effects of NP exposure on environment and human health. Although studies on NP genotoxicity already exist, few of them report *in vivo* data. In the present study, it was used the yeast *Saccharomyces cerevisiae* as a model to determine the genotoxic effect on the gametogenesis process of a particular kind of metal-based NPs, cadmium sulfide quantum dots (CdS QDs). CdS QDs cause a great alteration of the post-meiotic nuclear divisions with a strong inhibition of spore morphogenesis. Results obtained showed that CdS QDs cause an altered DNA content profile during the meiotic division, and a down-regulation of genes specifically expressed in the early-middle phase of the gametogenesis process and their downstream transcriptional targets. These results suggest that CdS QDs can inhibit progression through meiosis in an irreversible manner with adverse effects on meiotic cell cycle progression and spore formation.

Nanomaterials for tissue engineering and diagnostic applications: functionalization strategies and formulation opportunities

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The application of nanomaterials in Life Science include implantable medical devices, diagnostics and therapeutic nanosystems and smart tissue engineering scaffolds. Synthetic, natural and hybrid polymers can be opportunely modified to develop smart tools with tailorable properties. With this aim chemoselective methodologies can be applied to polymers of choice in order to control morphology, dimensions, biodegradability and bioactivity. In this talk, modification methodologies and synthetic strategies to develop smart nanomaterials will be presented with particular attention to the final applications. In particular, synthetic and natural polymers can be modified with crosslinkers to control stiffness and stability over the time, “bioactivated” with functional biomolecules to induce specific cell fates or linked to “bioresponsive” motifs (under pH, light, enzymes recognition control...) to control nanomaterials degradation or bioactivity in specific conditions. Examples of functionalized polymers to produce multimodal diagnostic nanoparticles and polymers for 3D in vitro models and tissue engineering applications will be presented [1, 2].

Acknowledgments:

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Novel stimuli-responsive nanocarriers for selected delivery of bioactive compounds in Craniosynostosis

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Nonsyndromic Craniosynostosis (NSC) is a rare craniofacial malformation, due to the premature fusion of one or more cranial sutures. Dysregulation of multiple signaling regulating the osteogenic stem cell fate in the fused suture is still partially unknown. The treatment of NSC is exclusively based on surgery; post-surgical relapses occur in about 10% cases and require re-interventions with associated risks for severe adverse effects.

We aimed at characterizing molecular mechanisms underlying the aberrant osteogenic properties of calvarial-derived mesenchymal stromal cells (CMSCs) within fused suture, in order to identify novel endogenous biomolecules to be exploited in the development of nanotechnologies for targeted therapies. Recombinant human ferritin (hFT) was tested as a suitable nanocarrier for targeted intracellular delivery upon binding to the transferrin receptor CD71, which is expressed in CMSCs. Further functionalized hFT-based construct was developed, with the N-terminus of each hFT subunit fused to a sequence, responsive to proteolytic cleavage by metalloproteases (MMPs) followed by an outer shielding polypeptide sequence. In this carrier the interaction between hFT and the receptor is then masked, being favored in the presence of MMP-enriched environment. Our preliminary results show that, upon osteogenic induction, the expression of MMP-9, -13 and 14 results higher in CMSCs isolated from fused suture. Optimization of hFT nanocarrier using a sequence cleaved by MMPs identified represents an innovative strategy to specifically target cells in the pathological skull suture using a stimuli-responsive delivery.

Future studies will address the upload of selected compounds able to reprogram the cell fate in the skull suture niche.

Regulation of mRNA expression in cells treated with CdS quantum dots

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Environmental exposure to nanomaterials is becoming more an issue as they are part of our life. As results more research on their effects at all level of ecological systems is needed. In particular the increasing environmental risk suggest to investigate more on the potential effect on human health. Here, we focused on CdS quantum dots (QDs), a nanomaterial with excellent optical properties used in different field as electronics, optoelectronics, in solar cells, pharmacy and nanomedicine for biomedical applications. The peculiar chemical-physical properties of nanomaterial influence their behavior in the biological system, therefore we have compared the effects of cadmium in nanometric form (CdS QDs) and in ionic form (Cd²⁺), which is well known its toxicity. At this purpose, RNA sequencing (RNAseq) was performed in two different cell lines which represent different target and routes of exposure. Both cell lines, HepG2 (liver hepatocellular carcinoma), and THP-1 (peripheral blood monocyte), were respectively treated with subtoxic dose of CdS QDs and Cd²⁺. The transcriptomic analysis data was performed and the different gene modulation reveals a cell type specific response to the two treatments. Notably, HepG2 cells are more sensitive to CdS QDs respect THP-1 that are involved to defense against exogenous substances. However, for both cell lines, a subtoxic dose of CdS QDs did not alter the normal cellular functions, whereas Cd²⁺, at the equivalent dose, induced a cellular stress response. The modulation of the different mRNA (up and down) was correlated with the regulation of their miRNAs as reported in the paper by Paesano *et al.* (submitted).

***In vitro* effects of ZnO and CuO NPs in mixture with DEP on A549 cells.**

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The main sources of ultrafine particles < 100 nm (UFPs) in urban areas and workplaces include combustion sources, especially diesel exhaust particles (DEP), but also non-exhaust sources or unintentional release of engineered nanoparticles (NPs). In a perspective of cumulative risk assessment is necessary to consider the possible interactive effects of different environmental stressor in biological systems. Commercially available (cZnO, cCuO < 50 nm) from Sigma-Aldrich) and sonochemically synthesized ZnO and CuO NPs (sZnO, sCuO), were used in mixtures with standard DEP (NIST 2975) to expose human lung A549 cells. NPs and mixtures were characterized by Transmission Electron Microscopy (TEM) and Dynamic Light Scattering (DLS). Cells were exposed for 24 h to mixtures consisting of DEP at a sub-toxic concentration and ZnO or CuO at increasing concentrations. At the end of the exposure, the cytotoxicity was assessed by MTT and Colony Forming Efficiency (CFE) assays, the Inflammatory response was evaluated using ELISA assay for Interleukin-8, and the cell morphology was investigated by fluorescence microscopy. The most hazardous single NPs resulted to be the cCuO ones, while the mixtures that more affect the viability were the DEP+ZnO ones. The different response towards DEP+sZnO and DEP+cZnO with respect to the individual ZnO NPs could be attributed to a possible different mechanism of interaction and endocytosis of the NMs once in mixture. In conclusion, by changing the physicochemical properties of NMs, the co-exposure with environmental UFP may modulate the biological responses. This aspect would be very useful for risk assessment and for the design of safer NMs.

From tailored molecules to advanced nanomaterials: the case porphyrins as active coatings for graphite electrodes surface protection

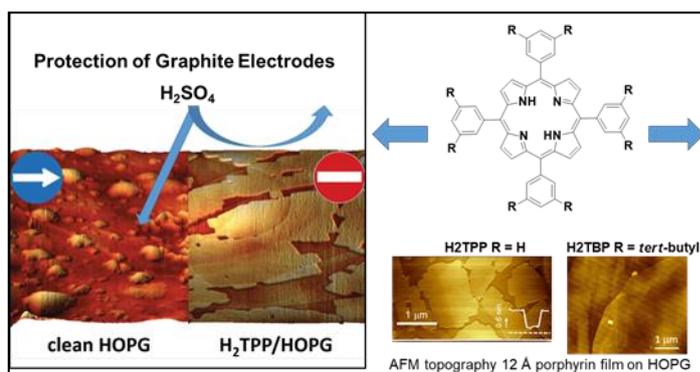
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The current development of optoelectronic and nanoscience technologies takes great advantage from the ability of organic compounds to fit precise needs and requirements of target applications. In this context, porphyrins represent an extremely interesting and versatile class of molecules; their organic framework can be easily chemically engineered, and their structure modified in order to tailor their optical and electrochemical features as well as their assembling behavior. Moreover, their chemical stability and ease of deposition via vacuum thermal evaporation, render porphyrins appealing as functional materials in ultrathin films and multilayer stacks with controllable properties. In this contribution, we describe the structure-property correlations of a series of metal-free tetra-phenyl-porphyrins (H₂TxP) with selected peripheral R substituents (Fig. 1) chosen to tune their steric, electronic and assembling features. We investigate H₂TxP both as (1) protective layer against graphite electrode degradation and as (2) highly absorbing materials in photovoltaics. In the case of graphite electrodes (1), employed in batteries and graphene production, they suffer from severe surface damages occurring under operation. Thin films of porphyrins were grown on the model highly oriented pyrolytic graphite (HOPG) surface. Employing *electrochemical-AFM* investigations we disclosed the blocking effect of H₂TPP (R=H) layer against the anion intercalation process in various acid electrolytes (Fig. 1 left). We later explored the effect of R groups on film blocking activity and disclose in this contribution.



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C.24 **Chemoselective functionalization of nanogels for selective cell treatments**

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Spinal cord injury (SCI) is an invalidating disease that involves the damage of the spinal cord or the nerves connecting the spine to the central and peripheral nervous system. This disease is characterized by the *primary SCI* that is the consequence of the primary traumatic event, and by the consequent inflammatory response, characterized by the activation of microglia/astrocytes, that leads to an aggravation of the pathology and it is responsible for neuro-degeneration and persisting pain state. A possible therapeutic approach is represented by the possibility to modulate the inflammatory response through the release of drugs and active compounds in the damaged zone. Recent studies in polymer science and nanotechnologies show an increased interest for the nanogels (NGs), a new class of colloidal systems that can be used as carriers of drugs to treat SCI.

In our work we investigate many functionalization strategies of nanogels, so that astrocytes, involved in the inflammatory response of SCI, can selectively internalize them limiting the uptake in microglia.

The nanogels were synthesized using polyethylene glycol (PEG) and polyethylene imine linear (PEI), after having functionalized the PEI with a chromophore using a “click” reaction. This functionalization is essential for being able to constantly trace the nanogels during the biological assays. Many different coating strategies (functionalization) of the nanogels were analysed considering the drug loading, the drug release and biocompatibility.

In vitro and *in vivo* biological tests have confirmed the potential of these functionalizations showing very good degree of internalization inside astrocytes limiting the uptake in microglia.

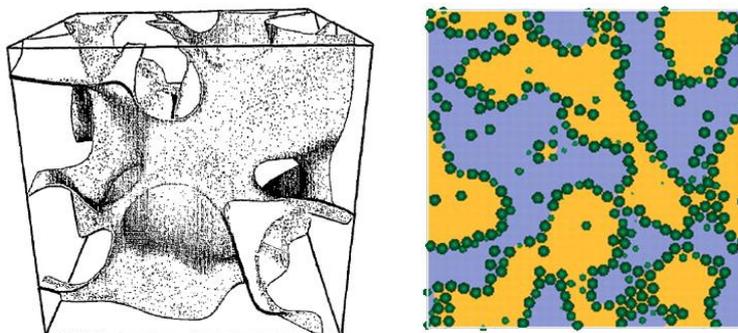
Nanoparticles as stabilizers of bijel-like structure for controlled drug delivery applications

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Bicontinuous interfacially jammed emulsion gels, or in simple terms *bijels*, are non-equilibrium structures formed by two non-mixable liquids, stabilized by a jammed layer of nanoparticles at the interface. Here nanoparticles have the same effects as surfactants, thus stabilizing emulsions, but gain the advantage of lower toxicity. These peculiar types of dispersions are the so-called Pickering emulsion [1]. They were theoretically discovered in 2005 through a computer simulation from Stratford et al. [2], trying to apply such properties towards two immiscible liquids. The first reproducible protocol for a tunable and three-dimensional bijel synthesis was developed later by Herzig et al. [3]. These peculiar products, thanks to their double nature, could be of interest for drug delivery applications, due to their ability of being loaded with both hydrophilic and hydrophobic drugs. The aim of this work is that of finding a synthetic route for the synthesis of bijel-like systems, where one species polymerizes during the production, leading to the formation of a creamy porous solid. The effect of different nanoparticles (both organic and inorganic) and synthesis parameters on the final product have been tested out. Furthermore, their ability to control the release of both hydrophilic and hydrophobic drug mimetics has been studied.



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Lead Halide Perovskite Nanoplatelets investigated by X-ray Total Scattering Methods

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Cesium Lead Halide perovskites CsPbX₃ (X = Cl, Br, I) nanocrystals exhibit attractive chemical-physical properties, in particular bright photoluminescence (PL, tunable over the entire visible spectral region by changing the halide composition), narrow bandwidths (<100 meV), high quantum yields (up to 100%) and short radiative lifetimes (1-29 ns) [1]. These features make them promising candidates for diverse advanced applications, such as lighting, displays, photovoltaics and lasing [2]. Fast and cheap colloidal syntheses were developed to manipulate size and shape of these materials at the nanoscale, leading to nanocubes, nanorods, nanosheets and nanoplatelets (NPLs) [3]. The latter exhibit good optical properties and strong quantum confinement effects on the absorption and emission energies, due to the presence of a very short dimension (a few unit cells thick) [4], which, ultimately, controls PL properties. In addition, NPLs have found good application as polycrystalline thin films in LEDs, thanks to the large surface area and their remarkable tendency to self-assemble [5]. Characterizing the structure and microstructure of these materials can be of fundamental importance to clarify the origin of such exceptional properties and to unveil new features [6]. Here, results of the analysis of highly stable blue-emitting CsPbBr₃ NPLs, performed by means of high resolution synchrotron X-ray total scattering techniques and a Debye scattering equation (DSE) [7] modelling, will be presented. As it will be illustrated, this method allows the complete characterization of structure, morphology, faceting, defects, size and size distribution of nanosized materials.

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