## **THE MISSION**



The **National Institute of Materials Physics (NIMP)** is proud to host the **9**<sup>th</sup> **International Workshop of Materials Physics (IWMP)**, centred around the theme "Advanced Materials and Methods for Healthcare and Pharmaceutical Industry".

The IWMP series is organized as an annual three-day event, scheduled to take place from May 14<sup>th</sup> to 16<sup>th</sup>, 2024. It will exclusively feature invited oral presentations and poster presentations.

The primary objective of the 9<sup>th</sup> edition of IWMP is to disseminate the latest scientific findings in advanced materials and characterization techniques in healthcare. The thematic focus includes biomaterials, the development of novel sensors for biomedical applications, and innovative approaches to drug formulation aimed at addressing drug instability.

The 9<sup>th</sup> edition of IWMP aims to attract prominent researchers from Europe and beyond, including Brazil, Czech Republic, France, Italy, Lithuania, the Netherlands, Portugal, Spain, the UK, and Romania. It serves as a platform for fostering new collaborations that may lead to joint publications, collaborative projects, and exchanges of personnel.

## THE VENUE



The Oteteleşanu Hall in Măgurele has a storied past dating back to the 19th century (1843), when it was built by the influential Oteteleşanu family. Initially serving as their private residence, it underwent a significant transformation in 1894, becoming the esteemed "Ioan Oteteleşanu Institute for Girls" under the auspices of the Romanian Academy.

Across its existence, the Otetelesanu Hall has stood witness to the dynamic evolution of Romanian history, from periods of subjugation at the cross-roads of three Empires to the victorious pursuit of independence and modernization. During its journey, the hall has endured three major wars, the vicissitudes of Communism, and the arduous path back to Democracy, navigating through cycles of transformation, neglect, and revitalization. Through it all, the Oteteleşanu Hall has remained a steadfast symbol of resilience amidst political turmoil and societal shifts.

Following a decade of careful restoration overseen by NIMP, Oteteleşanu Hall has been rejuvenated as the headquarters of the Culture and Physics Foundation in Măgurele, the International Centre for Advanced Training and Research in Physics (CIFRA), and the DRIFMAT cluster.

Today, it serves as a prestigious venue for international events like IWMP, embodying both its historical scope and contemporary relevance while upholding its unwavering, 130-years-old commitment to education and scientific advancement.

In the present day, the Oteteleşanu Hall stands as a testament to the cultural legacy of Măgurele, offering a captivating window into the past while remaining an integral part of the local community vibrant present.

### THE HOST

### NATIONAL INSTITUTE OF MATERIALS PHYSICS



Established in 1949, the Institute of Physics of the Romanian Academy was founded by Horia Hulubei, a distinguished scientist renowned for his ground-breaking contributions to various fields of physics, including Raman, X-rays, Compton, atomic, and nuclear physics. Hulubei earned his PhD in Paris under the tutelage of Nobel Prize laureates Pierre Curie and Maria Skłodowska-Curie.

In 1956, the Institute underwent a division resulting in the formation of two separate entities: the Institute of Atomic Physics (IFA) in Măgurele & the Bucharest Institute of Physics (IFB), the latter led by the Acad. Prof. Eugen Bădărău. E. Bădărău, a prominent professor from Sankt Petersburg and Cernăuți Universities, played a pivotal role in advancing the Romanian school of physics, particularly in the study of electrical discharges in gases and plasma.

Relocating to Măgurele in 1974, the Institute experienced further transformation in 1977 with the amalgamation of laboratories from IFB and IFA, forming the Institute of Physics and Technology of Materials. In 1996 it was officially rebranded the National Institute of Materials Physics (NIMP) following a national accreditation process, subsequently re-accredited in 2008 and 2016.

Throughout its history, NIMP has been home to distinguished physicists such as Acad. Eugen Bădărău, Acad. Radu Grigorovici, Acad. Ioan Iovitz Popescu, Acad. Margareta Giurgea, Acad. Rodica Mănăila, or Acad. Vladimir Țopa.

Over the past fifty years, NIMP has emerged as a leading research institution in Romania, investing over 35 million EUR in a new laboratory building equipped with state-of-the-art research facilities and the restoration of the historic Oteteleşanu Hall. Internationally, NIMP has played a significant role as one of the founders of the Central European Research Infrastructure (C-ERIC) and as an associated member of the Francophone University Agency (AUF). Additionally, it hosts a UNESCO category 2 centre – the Centre for Advanced Training and Research in Physics (CIFRA).

## **THE PROGRAM**

## of the 9<sup>th</sup> edition of the

## **International Workshop of Materials Physics**

14 May, 2024

## INVITED ORAL PRESENTATIONS

08:15	Registration – Oteteleșanu Hall			
08:45	Official opening – Lucian PINTILIE, Scientific Director of NIMP			
Session 1: Chairman –	Alexander KUHN			
09:00	Ifty AHMED			
	Faculty of Engineering, University of Nottingham, United Kingdom			
	Developing bioactive glasses and glass-ceramics for biomedical			
	applications			
09:30	Szilard FEJER			
	SC PROVITAM SRL, Romania			
	Research and development at a private healthcare institution:			
	Challenges and opportunities			
10:00	Raul-Augustin MITRAN			
	"Ilie Murgulescu" Institute of Physical Chemistry of the Romanian Academy,			
	Romania			
	Synthesis and characterization of <i>trans</i> -Resveratrol cocrystals			
10:30	Coffee Break			
10:45	Rabah BOUKHERROUB			
	Institut d'Electronique, de Microélectronique et de Nanotechnologie (IEMN),			
	France			
	Heat-induced controlled transdermal drug delivery for diabetes			
11.15	management			
11:15	Felix SIMA			
	Centre for Advanced Laser Technologies – CETAL, Romania			
	National Institute for Laser, Plasma and Radiation Physics – INFLPR,			
	Romania  Biochina with tailound volume chance febricated by ultrafact lease			
	Biochips with tailored volume shapes fabricated by ultrafast laser processing for cancer research			
11:45	Anton FICAI			
11.43	National University of Science and Technology POLITEHNICA Bucharest,			
	Romania			
	COLL/HA composite materials as drug-delivery systems in bone tissue engineering			
12:15	José M.F. FERREIRA			
12.13	Łukasiewicz Research Network – Institute of Microelectronics and Photonics.			
	Warsaw, Poland; University of Aveiro, Portugal			
	Design, development and characterisation of smart synthetic bone graft			
	materials for advanced therapies			
12:45	Lunch			

Session 2: Chairma	n – Rabah BOUKHERROUB			
14:00	Rasa PAULIUKAITE			
	Centre for Physical Sciences and Technology, Vilnius, Lithuania			
	Evolution of electrochemical sensors from macro to nano			
14:30	Camelia BALA			
	Department of Analytical Chemistry, University of Bucharest, Romania			
	Surface modification for label-free sensing			
15:00	Alexander KUHN			
	Institute of Molecular Science, University Bordeaux, France			
	Wireless Electrochemistry: From advanced materials to			
	(bio)electroanalysis and enantioselective synthesis			
15:30	Cecilia CRISTEA			
	"Iuliu Haţieganu" University of Medicine and Pharmacy, Romania			
	Development of innovative nano-systems for the targeted treatment of			
	cancer			
16:00	Coffee Break			
16:15	Posters Session			
17:15	Visit to NIMP's facilities, followed by Conference Dinner (19:00) at			
	"Caru' cu bere" Romanian Restaurant			

## 14 May, 2024

## POSTER PRESENTATION SESSION

Anca ALDEA <sup>1</sup> , Melania ONEA <sup>1,2</sup> , Daniela OPREA <sup>1,2</sup> , Daniel CRISAN <sup>1</sup> , Caroline SA <sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania <sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania  P2 Graphene electronic devices for sensing applications					
<sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania	Ionuţ				
	Ionuţ				
Y2   Graphene electronic devices for sensing applications	Ionuţ				
	Ionuţ				
Mariana Mihaela APOSTOL <sup>12</sup> , Elena MATEI <sup>1</sup> , Victor DICULESCU <sup>1</sup> ,					
ENCULESCU <sup>1</sup> , Issam BOUKHOUBZA <sup>1</sup>					
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
Technology POLITEHNICA Bucharest, 011061 Bucharest, Romania	<sup>2</sup> Faculty of Chemical Engineering and Biotechnologies, National University of Science and				
P3 Shape memory polymer nanofibres functionalized with PEDOT:PSS and Au nanopartic.	les for				
soft robotics applications	ics joi				
Mihaela BEREGOI <sup>1</sup> , Denisa CĂLIN <sup>2</sup> , Adrian ENACHE <sup>1</sup> , Ana Maria IGNAT <sup>1,3</sup> ,	Ionut				
ENCULESCU <sup>1</sup>	Ionuș				
<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania					
<sup>2</sup> Faculty of Medical Engineering, National University of Science and Techn	ology				
POLITEHNICA Bucharest, 011061 Bucharest, Romania	23				
<sup>3</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania					
P4 Paper-based electrochemical device integrated with conductive submicron polymeric fiber					
3D printed channels					
Daciana BOTTA <sup>1,2</sup> , Mihaela BEREGOI <sup>1</sup> , Alexandru EVANGHELIDIS <sup>1</sup> , Elena MA	TEI¹,				
Ionut ENCULESCU <sup>1</sup> , Victor DICULESCU <sup>1</sup>					
<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania					
<sup>2</sup> REOROM Laboratory, National University of Science and Technology POLITEHNICA					
Bucharest, 060042 Bucharest, Romania					
P5 The effect of fullerene layer on the aggregates formation in amyloid beta Langmuir-Bl	odgett				
films	1				
Carmen BREAZU <sup>1</sup> , Oana RAŞOGA <sup>1</sup> , Marcela SOCOL <sup>1</sup> , Paul GANEA <sup>1</sup> , Teddy T	TTE <sup>1</sup> ,				
Elena MATEI <sup>1</sup> , Florin STĂNCULESCU <sup>2</sup> , Anca STĂNCULESCU <sup>1</sup>					
<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania					
<sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania  P6 Soft actuators based on polydimethylsiloxane and electrospun fiber networks					
Mihaela-Cristina BUNEA, Mihaela BEREGOI, Alexandru EVANGHELIDIS, A	ndroi				
GALATANU, Ionut ENCULESCU	iluici				
National Institute of Materials Physics, 077125 Magurele, Romania					
P7 Nanohybrid composites of the type TiO <sub>2</sub> /single-walled carbon nanohorns for the Amox	icillin				
photodegradation					
Radu CERCEL <sup>1,2</sup> , Andreea ANDRONE <sup>1</sup> , Cristina-Ștefania FLORICA <sup>1</sup> , A	Adam				
LORINCZI <sup>1</sup> , Constantin SERBSCHI <sup>3</sup> , Mihaela BAIBARAC <sup>1</sup>					
<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania					
<sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania <sup>3</sup> S.C. Bioelec	etronic				
S.R.L., 100028 Ploiesti, Romania					
P8 Spectroscopic studies concerning degradation of Losartan Potassium					
Mădălina CHIVU <sup>1,2</sup> , Mirela PARASCHIV <sup>1,2</sup> , Ion SMARANDA <sup>1</sup> , Irina ZGURĂ <sup>1</sup> ,	Paul				
GANEA <sup>1</sup> , Bogdan CHIRICUȚĂ <sup>3</sup> , Mihaela BAIBARAC <sup>1</sup>					

	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	<sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania				
	<sup>3</sup> S.C. Apel Laser S.R.L., 077135 Mogosoaia, Romania				
P9	BT-based piezoceramics substituted with therapeutic cations				
	Marius Cristian CIOANGHER <sup>1</sup> , Liviu NEDELCU <sup>1</sup> , George E. STAN <sup>1</sup> , Luminita				
	AMARANDE <sup>1</sup> , Corneliu Florin MICLEA <sup>1</sup> , Adrian-Claudiu POPA <sup>1</sup> , Lucia Nicoleta				
	LEONAT <sup>1</sup> , Cristina BESLEAGA <sup>1</sup> , Cezar Dragos GEAMBASU <sup>1</sup> , Vasilica TOMA <sup>1</sup> , Irina				
	Sorina GHITA <sup>1</sup> , Robert Catalin CIOCOIU <sup>2</sup> , Constantin MARIN <sup>3</sup>				
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	<sup>2</sup> Department of Metallic Materials Science, National University of Science and Technology				
	POLITEHNICA Bucharest, 060042 Bucharest, Romania				
	<sup>3</sup> "Emil Racovită" Institute of Speleology of the Romanian Academy, 050711 Bucharest, Romania				
P10	Yttrium barium copper nano oxide synthesis for biomedical utilization				
	Rania DAHA <sup>1</sup> , Manel BOULOUDENINE <sup>2,3</sup> , Katia DJENADi <sup>4</sup> , Stefano BELLUCCI <sup>5</sup>				
	<sup>1</sup> École Nationale Supérieure des Mines et de la Métallurgie (ENSMM)-Amar Laskri, L3M,				
	Chainz, 23000 Annaba, Algeria				
	<sup>2</sup> Mohamed-Cherif Messaadia University, 41000 Souk Ahras, Algeria				
	<sup>3</sup> LPR, Laboratory, University Badji Mokhtar, 23000 Annaba, Algeria				
	<sup>4</sup> Laboratoire de Biochimie Appliquée, Département des Sciences Alimentaires, Faculté des				
	Sciences de la Nature et de la Vie, Université de Bejaia, 06000 Bejaia, Algeria				
	<sup>5</sup> INFN-Laboratori Nazionali di Frascati, 00044 Frascati, Italy				
P11	Photodegradation of aspirin and atorvastatin calcium revealed by photoluminescence studies				
	Monica DĂESCU <sup>1</sup> , Miruna IOṬA <sup>1</sup> , Alina C. ION <sup>2</sup> , Constantin SERBSCHI <sup>3</sup> , Mihaela				
	BAIBARAC¹, Mădălina OPRICĂ¹, Szilard FEJER⁴				
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	<sup>2</sup> Faculty of Chemical Engineering and Biotechnologies, National University of Science and				
	Technology POLITEHNICA Bucharest, 011061 Bucharest, Romania				
	<sup>3</sup> S.C. Bioelectronic S.R.L., 100028 Ploiesti, Romania				
	<sup>4</sup> Pro-Vitam Ltd., 520032 Sfantu Gheorghe, Romania				
P12	Electrospun fibrillary scaffold for electrochemical cell biomarkers detection				
	Adrian ENACHE <sup>1</sup> , Mihaela BEREGOI <sup>1</sup> , Daniela OPREA <sup>1,2</sup> , Mihaela Cristina BUNEA <sup>1</sup> ,				
	Monica ENCULESCU <sup>1</sup>				
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	<sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania				
P13	Electron beam synthesis of iron oxide nanoparticles for biomedical applications				
	Nicusor IACOB¹, Cezar COMANESCU¹, Gabriela CRACIUN², Andrei C. KUNCSER²,				
	Cristian RADU <sup>1</sup> , Petru PALADE <sup>1</sup> , Elena MANAILA <sup>2</sup> , Gabriel SCHINTEIE <sup>1</sup> , Daniel				
	IGHIGEANU <sup>2</sup> , Victor KUNCSER <sup>1</sup>				
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	<sup>2</sup> National Institute for Laser, Plasma and Radiation Physics, 077125 Magurele, Romania				
P14	A computational perspective on the fundamental aspects of magnetic hyperthermia				
	Andrei C. KUNCSER <sup>1</sup> , Cristian RADU <sup>1,2</sup> , Ioana D. KUNCSER <sup>1</sup>				
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	<sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania				
P15	Reliable evaluation of drug loading degree of Fe oxide nanoparticles by combined Mössbauer				
110	Spectroscopy and Magnetometry				
	Victor KUNCSER <sup>1</sup> , Petru PALADE <sup>1</sup> , Gabriel SCHINTEIE <sup>1</sup> , Cezar COMANESCU <sup>1</sup> ,				
	Nicusor IACOB¹, Luiza-Izabela TODERASCU², Gabriel SOCOL²				
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	1 miles in the contraction of th				

	<sup>2</sup> National Institute for Laser, Plasma and Radiation Physics, 077125 Magurele, Romania
P16	Cytotoxicity and biotransformation of Cerium Oxide-Iron Oxide platform in cells cultures and
F 10	murine model
	Valentin-Adrian MARALOIU <sup>1</sup> , Catalina MIHALCEA <sup>1,2</sup> , Cristian RADU <sup>1,2</sup> , Yuliia
	SHLAPA <sup>3</sup> , Anatolii BELOUS <sup>3</sup> , Aida SELARU <sup>4</sup> , Sorina DINESCU <sup>4</sup> , Cosmin
	MUSTACIOSU <sup>5</sup>
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania
	<sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania
	<sup>3</sup> V.I. Vemadsky Institute of General & Inorganic Chemistry of the NAS of Ukraine, 03142 Kiev,
	Ukraine
	<sup>4</sup> Department of Biochemistry and Molecular Biology, University of Bucharest, 050095 Bucharest,
	Romania
	<sup>5</sup> Horia Hulubei National Institute for Physics and Nuclear Engineering, 077125 Magurele,
	Romania
P17	Optical evidence of photodegradation of azathioprine under UV irradiation in an oxygen
11/	atmosphere
	Andreea NILĂ <sup>1</sup> , Ion SMARANDA <sup>1</sup> , Corina-Mihaela MANTA <sup>2</sup> , Dumitru
	SAMOHVALOV <sup>2</sup> , Daniel GHERCA <sup>2</sup> , Mihaela BAIBARAC <sup>1</sup>
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania
	<sup>2</sup> S.C. Sara Pharm Solutions S.R.L., 050122 Bucharest, Romania
P18	Antioxidant properties assessment of spring greens used in traditional Romanian green salad
110	Daniela OPREA <sup>1,2</sup> , Daniel CRISAN <sup>1</sup> , Adrian ENACHE <sup>1</sup>
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania
	<sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania
P19	Photoactive and magnetoactive nanocomposites for biomedical applications
	Traian POPESCU <sup>1</sup> , Ioana D. KUNCSER <sup>1</sup> , Valentin-Adrian MARALOIU <sup>1</sup> , Monica
	ILAS <sup>1</sup> , Arpad Mihai ROSTAS <sup>1,2</sup> , Alexandra-Corina IACOBAN <sup>1</sup> , Nicusor IACOB <sup>1</sup> ,
	Christien Oktaviani MATEI <sup>3</sup> , Tudor SAVOPOL <sup>3</sup> , Mihaela G. MOISESCU <sup>3</sup>
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania
	<sup>2</sup> National Institute of Isotopic and Molecular Technologies, 400293 Cluj-Napoca, Romania
	<sup>3</sup> Department of Biophysics and Cellular Biotechnology, Carol Davila University of Medicine and
	Pharmacy, 050474 Bucharest, Romania
P20	Preparation, analysis, and antibacterial properties of magnesium doped hydroxyapatite
	suspensions
	Daniela PREDOI, Simona Liliana ICONARU, Steluta Carmen CIOBANU, George E.
	STAN
	National Institute of Materials Physics, 077125 Magurele, Romania
P21	Evaluation of shape anisotropy in nanoparticles for magnetic hyperthermia
	Cristian RADU <sup>1,2</sup> , Ioana D. KUNCSER <sup>1</sup> , Andrei C. KUNCSER <sup>1</sup>
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania
	<sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania
P22	Controlling the shape and particle size distributions of magnetic nanoparticles prepared by
	thermal decomposition of organometallic compounds
	Gabriel SCHINTEIE, Andrei C. KUNCSER, Nicusor IACOB, Cezar COMANESCU,
	Victor KUNCSER
	National Institute of Materials Physics, 077125 Magurele, Romania
P23	MgB2-based materials for biomedical applications
	Any-Cristina SERGENTU <sup>1,2</sup> , Petre BADICA <sup>1</sup>
	<sup>1</sup> National Institute of Materials Physics, 077125, Magurele, Romania

	<sup>2</sup> National University of Science and Technology POLITEHNICA Bucharest, 060042 Bucharest,				
	Romania				
P24	Effects of pH and UV radiation on the optical properties of folic acid in phosphate buffer				
	solutions				
	Ion SMARANDA <sup>1</sup> , Andreea NILA <sup>1</sup> , Mihaela BAIBARAC <sup>1</sup> , Constantin SERBSCHI <sup>2</sup>				
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	<sup>2</sup> S.C. Bioelectronic S.R.L., 100028 Ploiesti, Romania				
P25	Ferromagnetic shape memory ribbons as potential active elements in stent-type medical devices				
	Mihaela SOFRONIE <sup>1</sup> , Felicia TOLEA <sup>1</sup> , Bogdan POPESCU <sup>1</sup> , Mugurel TOLEA <sup>1</sup> , Mihaela				
	VALEANU <sup>1</sup> , Alexandrina NAN <sup>2</sup> , Alexander BUNGE <sup>2</sup> , Rodica TURCU <sup>2</sup> , Alexandru				
	CHIRIAC <sup>3</sup>				
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	<sup>2</sup> National Institute for Research and Development of Isotopic and Molecular Technologies,				
	400293 Cluj-Napoca, Romania				
	<sup>3</sup> University of Medicine and Pharmacy Grigore T. Popa, 700115 Iasi, Romania				
P26	Copper & Gallium co-substituted bioactive glasses: Path towards durable dental implant				
	coatings				
	George E. STAN <sup>1</sup> , Teddy TTTE <sup>1</sup> , Adrian-Claudiu POPA <sup>1</sup> , Maria-Iuliana CHIRICA <sup>1</sup> ,				
	Cristina BESLEAGA <sup>1</sup> , George LUNGU <sup>1</sup> , Irina ZGURA <sup>1</sup> , Catalin NEGRILA <sup>1</sup> , Daniel				
	CRISTEA <sup>2</sup> , Cristiana TANASE <sup>3</sup> , José M.F. FERREIRA <sup>4</sup>				
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	<sup>2</sup> Transilvania University of Brasov, 500068 Brasov, Romania				
	<sup>3</sup> "Victor Babes" National Institute of Pathology, 050096 Bucharest, Romania				
	<sup>4</sup> CICECO—Aveiro Institute of Materials, Department of Materials and Ceramics Engineering,				
D0=	University of Aveiro, 3810-193 Aveiro, Portugal				
P27	The potential applications of the polyaniline/carbon nanoparticles composites in the				
	azathioprine detection				
	Adelina UDRESCU, Mihaela BAIBARAC, N'Ghaya TOULBE, Elena MATEI				
P28	National Institute of Materials Physics, 077125 Magurele, Romania				
P28	Composites based on reduced graphene oxide for medical applications Mirela VĂDUVA, Mihaela BAIBARAC				
	National Institute of Materials Physics, 077125 Magurele, Romania				
P29	Composites based on biogenic Silver, Gold, Silver Chloride and Zinc Oxide Structures as green				
P29	composues based on biogenic Suver, Goid, Suver Chioride and Zinc Oxide Structures as green multifunctional platforms for biomedical applications				
	Irina ZGURA <sup>1</sup> , Monica ENCULESCU <sup>1</sup> , Valentin-Adrian MARALOIU <sup>1</sup> , Cosmin				
	ISTRATE <sup>1</sup> , Raluca NEGREA <sup>1</sup> , Liviu NEDELCU <sup>1</sup> , Nicoleta BADEA <sup>2</sup> , Camelia				
	UNGUREANU <sup>2</sup> , Marcela-Elisabeta BARBINTA-PATRASCU <sup>3</sup> , Mihaela BACALUM <sup>4</sup>				
	<sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
	<sup>2</sup> Faculty of Chemical Engineering and Biotechnologies, National University of Science and				
	Technology POLITEHNICA Bucharest, 011061 Bucharest, Romania				
	<sup>3</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania				
	<sup>4</sup> Department of Life and Environmental Physics, Horia Hulubei National Institute for Physics and				
	Nuclear Engineering, 077125 Magurele, Romania				
P30	Nanostructured human serum albumin as drug delivery carrier to cancer cells				
150	Claudia. G. CHILOM <sup>1</sup> , Sorina IFTIMIE <sup>1</sup> , Adriana E. BALAN <sup>1</sup> , Teodor A. ENACHE <sup>2</sup> ,				
	Daniela OPREA <sup>1,2</sup> , Monica ENCULESCU <sup>2</sup>				
	<sup>1</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania				
	<sup>2</sup> National Institute of Materials Physics, 077125 Magurele, Romania				
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## 15 May, 2024

## INVITED ORAL PRESENTATIONS

Session 3: Chairman – J	osé M.F. FERREIRA				
09:00	Fabiana ARDUINI				
	Department of Chemical Science and Technologies, University of Rome				
	"Tor Vergata", Italy				
	Paper-based printed electrochemical (bio)sensors as smart and				
	sustainable point-of-care devices				
09:30	Antonia PAJARES VICENTE				
	Department of Mechanical, Energy and Materials Engineering, University of				
	Extremadura, Spain				
	Improving the mechanical performance of bioceramic scaffolds for				
	biomedical applications				
10:00	Pedro MIRANDA GONZÁLEZ				
	Department of Mechanical, Energy and Materials Engineering, University of				
	Extremadura, Spain				
	Leveraging the high resolution of digital light processing in the additive				
	manufacturing of high-performance composites for biomedical				
	applications				
10:30	Mihaela MOISESCU				
	Department of Biophysics and Cellular Biotechnology, Faculty of Medicine,				
	University of Medicine and Pharmacy "Carol Davila", Romania				
	Nano-biomaterials' interactions with cells: Challenges and opportunities				
11:00	Coffee Break				
11:15	Lucian BAIA				
	Faculty of Physics, Babes-Bolyai University, Romania				
	Composites based on biopolymers-bioactive glasses/glass-ceramics				
	containing Cu and Au for tissue engineering applications				
11:45	Jeroen VAN DEN BEUCKEN				
	Radboud University Medical Centre, Netherlands				
10.15	Steering biological processes to stimulate bone formation				
12:15	Daniela-Cristina BERGER				
	National University of Science and Technology POLITEHNICA Bucharest,				
	Romania				
10.45	Biocomposites based on functionalised mesoporous silica				
12:45	Lunch				
	eroen VAN DEN BEUCKEN				
14:00	Stefano BELLUCCI				
	INFN—Laboratori Nazionali di Frascati, Italy				
14.20	Nanomaterials for health science applications				
14:30	Monica BAIA				
	Faculty of Physics, Babes-Bolyai University, Romania				
15.00	Raman and SERS investigations on pharmaceuticals				
15:00	Josef JAMPÍLEK – on-line presentation				
	Faculty of Science, Palacky University in Olomouc, Czech Republic				
	Drug delivery nanosystems for modern targeted therapy				

15:30	Coffee Break			
16:00	Simion AȘTILEAN			
	Faculty of Physics, Babes-Bolyai University, Romania			
	Plasmonic-based nanoplatforms for light-activated therapy, bioimaging			
	and sensing			
16:30	Orlando FATIBELLO-FILHO – on-line presentation			
	Department of Chemistry, São Carlos Federal University, Brazil			
	Modified electrodes with nanostructured carbon and/or metallic			
	composites for applications in electroanalysis			
17:00	Commute to the Hotel Moxy			
18:30	Sightseeing tour of Bucharest starting from Hotel Moxy, followed by			
	Conference Dinner (20:00) at Linea/Closer to the Moon rooftop venue.			

## 16 May, 2024

## INVITED ORAL PRESENTATIONS

Session 5: Chairman –	Simion AȘTILEAN				
09:00	Mihaela DONI				
	National Institute for Research & Development in Chemistry and				
	Petrochemistry, Romania				
	Biosensing approaches for development of innovative analytical systems				
	for agriculture, food and environmental fields				
09:30	Gabriela GRAZIANI				
	Polytechnic University of Milan, Italy				
	Nanostructured antibacterial films by Ionized Jet Deposition: An				
	overview				
10:00	Monica FLORESCU				
	Department of Fundamental, Prophylactic and Clinical Disciplines, Faculty of				
	Medicine, Transilvania University of Braşov, Romania				
	Functional nanostructured materials for biomedical applications				
10:30	Coffee Break				
11:00	Marc Lamy DE LA CHAPELLE				
	Université du Mans, France; Babes-Bolyai University, Romania				
	Detection, identification and structural study of biomolecules by Surface				
	Enhanced Raman Spectroscopy				
11:30	Mariana Carmen CHIFIRIUC / Grațiela GRĂDIȘTEANU				
	Faculty of Biology, University of Bucharest, Romania				
	Novel therapeutic approaches for the management of malignant wounds				
12:00	Casan-Pastor NIEVES – on-line presentation				
	Institute of Materials Science of Barcelona, Spain				
	Redox gradients in materials and unwired bipolar electrodes in neural				
	systems				
12:30	CONCLUDING REMARKS				
13:00	Lunch				

## Abstracts of Invited Oral Presentations

#### Developing Bioactive Glasses and Glass-Ceramics for Biomedical Applications

#### Ifty AHMED

Faculty of Engineering, University of Nottingham, Nottingham, NG7 2RD, United Kingdom ifty.ahmed@nottingham.ac.uk

The initial interest in our group was exploring use of phosphate-based glasses as fully resorbable biomaterials. These glass-based biomaterials offer wide ranging and controlled degradation profiles (from day/s, week/s to many months) by simply manipulating their chemical formulations. Phosphate-based glasses are unique biomaterials, as their chemical composition can be made to resemble the mineral content of natural bone, providing excellent cytocompatibility.

Interest in developing resorbable medical devices has increased over recent years. Initially we explored PLA and PCL polymer matrices to produce implantable medical devices, such as fully resorbable bone fracture fixation plates (see Fig. 1a,b). However, the mechanical properties of polymers alone are insufficient to be used in higher load bearing applications. For example, the modulus of cortical bone in longitudinal direction is  $\sim$ 17.7 GPa [1], whilst those of typical polymeric biomaterials can range between 1 – 5 GPa [2]. Our potential solution to this problem was to reinforce these polymers with high modulus bioactive glass fibres. As such, phosphate-based glass fibres (PGFs) containing calcium were used as the main advantage was that these fibrous materials were also fully biodegradable and possessed sufficient mechanical strength for bone repair (tensile tests demonstrated  $E\approx$ 65+ GPa [3–4]) (see Fig. 1c,d).

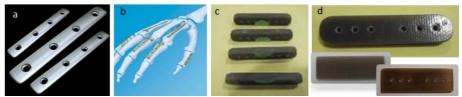


Fig. 1. (a,b) Depiction of metal plates used for bone fracture repair; (c,d) Examples of resorbable composite plates developed in our group [1–3].

In the last few years, we have also been developing fully resorbable solid/dense (non-porous) and highly porous glass microspheres from phosphate-based glasses for regenerative medicine and other biomedical applications. Manufacturing porous microspheres from glass-based materials with nano- to micron-range porosity has huge potential in bone repair and regeneration applications where larger external pores within the microspheres could accommodate cells and the smaller pores could be utilised to encapsulate other types of biological components such as drugs, small molecules, nucleic acids, proteins, *etc*.

Our group was the first to successfully develop a single-stage manufacturing process for producing solid (non-porous) and highly porous microspheres [5,6] from calcium phosphate-based glasses (see Figs. 2a–d), which has now also been demonstrated for alternate glass systems such as silicates and borates [7,8]. Follow-on studies confirmed that the porous microspheres had both large surface and fully inter-connected porosity (as shown in Figs. 2e,f). Further studies also confirmed that human mesenchymal stem cells not only attached to the microspheres, but also migrated to reside within their pores (see Fig. 2g).

More recently, we have been developing biomaterials for bone cancer and radiotherapy applications which led to manufacture of novel glass ceramic biomaterial. We also managed to incorporate magnetic properties in some biomaterials with potential application for hyperthermia. These will also be briefly highlighted during the presentation.

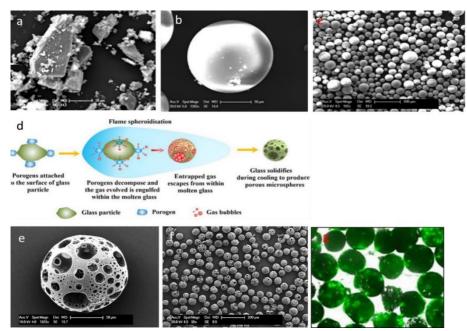


Fig. 2. (a-c) Starting particles processed as solid/dense microspheres; (d) Scheme of developed manufacturing process; (e-g) Highlights of porous glass microspheres produced and stem cell attachment [5,6].

- [1] J. Currey, Cortical bone, in: Handbook of Biomaterial Properties, J. Black and G. Hastings, Eds., Springer US, 1998, pp. 3–14.
- [2] S. Ramakrishna, J. Mayer, E. Wintermantel, et al., Compos. Sci. Technol. 2001, 61, 1189–1224.
- [3] K. Hossain, R. Felfel, D. Grant, I. Ahmed, Phosphate glass fibres and their composites, in: Bioactive Glasses: Fundamentals, Technology and Applications, A.R. Boccaccini, D. Brauer, L. Hupa, Eds., Royal Society of Chemistry, 2017, pp. 257–285.
- [4] M. Chen, A.J. Parsons, R.M. Felfel, et al., J. Mech. Behav. Biomed. Mater. 2016, 59, 78–89.
- [5] K.M.Z. Hossain, U. Patel, I. Ahmed, *Prog. Biomater.* **2015**, *4*, 1–19.
- [6] K.M.Z. Hossain, U. Patel, A.R. Kennedy, et al., Acta Biomater. 2018, 72, 396–406.
- [7] M.T. Islam, L. Macri-Pellizzeri, V. Sottile, et al., Biomater. Sci. 2021, 9, 1826–1844.
- [8] M.T. Islam, N.A. Nuzulia, L. Macri-Pellizzeri, et al., J. Biomater. Appl. 2022, 36, 1427–1443.

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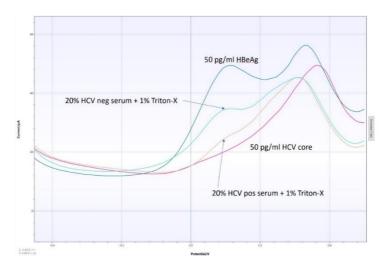
## Research and Development at a Private Healthcare Institution: Challenges and Opportunities

#### Szilard FEJER

Pro-Vitam Diagnostics and Research Centre, 520032 Sfantu Gheorghe, Romania fejerszilard@provitam.com

The research ecosystem in Romania has been always struggling with securing the necessary funding. During the last few years, private companies also started investing in R&D activities. However, for private healthcare providers, such endeavours carry high risks, but also very rewarding opportunities. I will present the journey of our small healthcare business in creating a research lab and growing it over the years, by seizing opportunities in the field of developing new diagnostic devices and fostering collaborations with public research institutions.

The SARS-CoV-2 pandemic was a huge challenge worldwide. Our lab developed the first and only Elisa assay for detecting COVID-19 antibodies that was registered as a CE IVD device in Romania. With the lucky combination of a dedicated research team and readily available clinical samples, we adjusted our research goals to also develop diagnostic devices for hepatitis C core protein and anti-hepatitis Delta antibody detection as well. We also assessed the possibility of developing biosensors for such antibody detection, with mixed results. Our most promising results in this field involve gold nanoparticles functionalized with covalently linked virus antigens, using square wave voltammetry for antibody detection in clinical samples.



Example SWV graph for biosensors functionalized with covalently linked anti-HCV core antibodies, incubated with samples containing either HCV core antigen or an irrelevant antigen (HBeAg) or a serum sample negative for HCV infection.

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### Synthesis and Characterization of Trans-Resveratrol Cocrystals

Raul-Augustin MITRAN $^{1,*}$ , Simona IONIȚĂ $^1$ , Daniel LINCU $^1$ , Irina ATKINSON $^1$ , Mariana PĂTRASCU $^2$ , Elena Mirabela SOARE $^1$ , Adriana RUSU $^1$ , Jeanina PANDELE-CUȘU $^1$ , Coca IORDACHE $^3$ , Victor FRUTH $^1$ 

The rise of antibiotics resistance is a global health threat in the 21st century, which is partially caused by the overuse of antibiotics in both humans and farm animals. It is estimated that 73% of worldwide antibiotics are used for livestock animals, such as pigs, cows and poultry, with pigs consuming the largest amount of antibiotics [1]. Plant extracts have recently gained traction as a potential functional alternative to antibiotics in livestock production [2]. The active ingredients are comprised of polysaccharides, polyphenols, alkaloids etc. Trans-Resveratrol (3,5,4'-trihydroxy-trans-stilbene) is a natural polyphenol which exhibits a range of useful biological properties, such as antioxidant, anticancer, antiangiogenic, cardioprotective and immunomodulatory activities. However, Resveratrol suffers from limited solubility and chemical stability, which prevents its widespread use.

Solid form modifications can be used to enhance desired properties of active pharmaceutical ingredients. Cocrystals formation represents a promising alternative to other solid form modifications (amorphization, polymorphs, *etc*) since it results in thermodynamically stable, crystalline compounds. Cocrystals exhibit unique physical properties, which can impact key pharmaceutical parameters, including storage stability, compressibility, density as well as dissolution rates and solubility, which are essential factors in achieving suitable bioavailability.

The aim of this study is the investigation of different synthesis pathways to obtaining a 1:1 (mol.) Resveratrol: Piperazine cocrystal, using methods amenable to large scale production. These methods include mechanochemical ultrasound or microwave assisted synthesis.

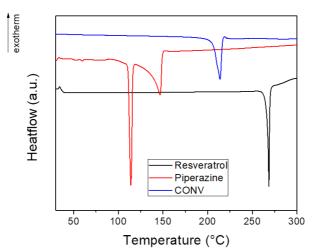


Fig. 1. DSC data of cocrystal and coformers.

<sup>&</sup>lt;sup>1</sup> "Ilie Murgulescu" Institute of Physical Chemistry, Romanian Academy, 060021 Bucharest, Romania

<sup>&</sup>lt;sup>2</sup> Research & Development Department, Primosal Srl, 060886 Bucharest, Romania

<sup>&</sup>lt;sup>3</sup> TeraCrystal SRL, 67–103 Donat, 400293 Cluj Napoca, Romania

<sup>\*</sup>raul.mitran@gmail.com

Different synthesis conditions (the nature and amount of added solvent, reaction time and temperature) were investigated and their influence on the cocrystal phase and purity were determined, using thermal analysis (Fig. 1), X-ray powder diffraction and infrared spectroscopy methods. The solubility of the cocrystals obtained through different methods was assessed. Ethanol assisted mechanochemical synthesis, as well as microwave and ultrasound assisted methods provided the desired cocrystal phase with high purity and yield.

**Acknowledgments:** This work was supported by a grant of the Romanian Ministry of Education and Research, CNCS-UEFISCDI, project number PN-III-P2-2.1-PTE-2021-0393, contract number PTE 98/2022.

- [1] K. Tiseo, L. Huber, M. Gilbert, et al., Antibiotics, 2020, 9, 918.
- [2] M. Piao, Y. Tu, N. Zhang, et al., Antioxidants, 2023, 12, 879.

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### Heat-induced Controlled Transdermal Drug Delivery for Diabetes Management

## Alexandre BARRAS, Valérie PLAISANCE, Valérie PAWLOWSKI, Amar ABDERRAHHMANI, Sabine SZUNERITS, Rabah BOUKHERROUB\*

Institute of Electronics, Microelectronics and Nanotechnology (IEMN), UMR CNRS8520, 9652 Villeneuve d'Ascq, France

Diabetes is defined as a chronic elevation of glycemia. Due to acute and chronic complications, the disease poses a major economic, social, and medical burden on society worldwide. Diabetes is characterized by insufficient insulin plasma level to meet the organism demand. In type 1 diabetes, absolute deficiency of insulin production results from massive auto-immune destruction of pancreatic beta cells. For this reason, the main therapy consists in delivering exogenous insulin. The treatment methods require numerous daily injections of insulin administered by subcutaneous needle injection, insulin pen and catheters connected to insulin pumps. These methods are, however, both painful and inconvenient as the invasive multiple injections of precisely calculated amounts of insulin present a significant deterioration of the life quality of the diabetic patients. The discomfort associated with this type of administration has led diabetic patients to neglect or even give up the therapy. There is, thus, an increasing demand for the design of new insulin administration systems and this has led to the investigations of oral, nasal, buccal, pulmonary, rectal, ocular and transdermal routes.

Transdermal delivery of insulin, a simple and painless method, represents a viable alternative for the controlled release of insulin over time together with high patience compliance. However, transdermal delivery is limited by the low permeability of the stratum comeum, the skin outermost layer, allowing only small (<500 Da) hydrophobic molecules to be delivered. In this presentation, I will discuss our original contribution on insulin transdermal delivery upon photothermal or electrothermal activation.

- [1] A. Voronova, M. Pardo-Figuerez, J.M. Lagaron, et al., ACS Applied Bio Materials 2022, 5, 771–778.
- [2] B. Demir, L. Rosselle, A. Voronova, et al., Nanoscale Horiz. 2022, 7, 174-184.
- [3] S. Szunerits, S. Melinte, A. Barras, et al., Chem. Soc. Rev. 2021, 50, 2102–2146.
- [4] Q. Pagneux, R. Ye, L. Chengnan, et al., Nanoscale Horiz. 2020, 5, 663-670.
- [5] S. Szunerits, R. Boukherroub, Front. Bioeng. Biotechnol. 2018, 6, 151.
- [6] F. Teodorescu, Y. Oz, G. Queniat, etal., J. Control. Release 2017, 246, 164–173.

<sup>\*</sup>rabah.boukherroub@univ-lille.fr

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## Biochips with Tailored Volume Shapes Fabricated by Ultrafast Laser Processing for Cancer Research

## Felix SIMA<sup>1,2\*</sup>, Kotaro OBATA<sup>2</sup>, Mirai HANZAWA<sup>2</sup>, Hiroyuki KAWANO<sup>2</sup>, Florin JIPA<sup>2</sup>, Alexandra BRAN<sup>2</sup>, Emanuel AXENTE<sup>2</sup>, Koji SUGIOKA<sup>2</sup>

<sup>1</sup>CETAL, National Institute for Laser, Plasma and Radiation Physics, 077125 Magurele, Romania

Lab-on-a-chip strategies are using miniaturized devices that enable cells to be cultured for subsequent studies in tridimensional (3D) spaces mimicking *in vivo* environment. Configurations relevant for specific tissues at adequate conditions of temperature and pH can be architected. This could allow live observation of cells with a high microscopic resolution over long time periods that are of great interest for *e.g.* cancer cell migration studies.

Ultrafast lasers, defined as lasers emitting pulsed beams with durations shorter than few picoseconds, are used nowadays for such Lab-on-a-chip devices. The extremely high peak intensity associated with ultrashort pulse width allows to induce nonlinear interaction such as multiphoton absorption with materials that are transparent to the laser wavelength. By focusing the ultrashort laser beams inside transparent materials one may confine the nonlinear interaction only within the focal volume, enabling 3D micro- and nanofabrication. We apply subtractive 3D processing technologies including femtosecond laser assisted chemical etching (FLAE) and picosecond laser assisted chemical etching (PLAE) to develop 3D microfluidic networks embedded in photosensitive glass microchips [1,2]. We have thus developed graded and hierarchical configurations with dimensions from hundreds of micrometres to hundreds of nanometres as relevant glass model platforms that mimic cancer cell intravasation-extravasation processes. The fabricated biochip provides 3D hierarchical architectures with nanoscale characteristics and an ultrathin (<100  $\mu$ m) chip base for high-resolution live cell imaging (Fig. 1).

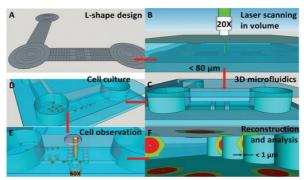


Fig. 1. Sequential procedure of glass micro/nanofluidic biochip fabrication and study of cancer cell invasion and migration in the fabricated narrow constructive spaces. (a) 2D design for laser direct writing scheme. The focused laser beam is scanned along the solid lines. (b) Laser direct writing process in the glass volume according to the design shown in a. To produce a 3D configuration, multiple layers were scanned according to the 2D model by shifting the focused laser beam along the beam axis. (c) 3D micro/nanofluidic structures obtained after chemical wet etching and post-thermal treatment. (d) Cell culturing: loading cells into the micro-reservoir. (e) Time-lapse fluorescence observation of cancer cell invasion and migration within narrow constrictive spaces between pillars. (f) Image recording, reconstruction, and analysis.

<sup>&</sup>lt;sup>2</sup>RIKEN Center for Advanced Photonics, 351-0198, Saitama, Japan

<sup>\*</sup>felix.sima@inflpr.ro

Nanochannels narrower than 1  $\mu m$  with a height of 6.75  $\mu m$  and a length of over 50  $\mu m$  were developed inside the glass. Prostate cancer (PC3) cells were cultivated and grown inside the glass biochip, and migration and invasion of the cultivated cells in narrow spaces were then observed by high-resolution live cell imaging using confocal time-lapse microscopy. Such biochips proved capability of offering both observation of collective prostate cancer cells migration over long time periods and individual visualization at unicellular and subcellular levels on the target cell [3] (Fig. 2).

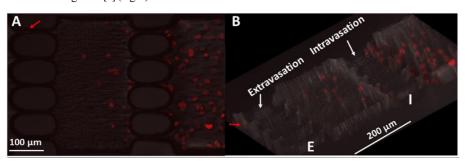


Fig. 2. Cell migration and invasion in nanochannels: confocal fluorescence images of cell nuclei merged with optical images. (a) Top-down view and (b) reconstructed bird's-eye view showing that the first cell (indicated by a red arrow) is invading the second row of pillars (E-row).

Miniaturized lab-on-chip glass platforms were further developed to simultaneously perform dosimetry measurements and evaluation of biological effects of ionizing radiation on cancer cells [4]. We designed and fabricated a tumour-on-chip model platform consisting of co-cultures of melanoma and melanocytes cells grown in a laser processed glass microenvironment that allowed to discriminate the radiation effect on cancer cells vs. normal tissue cells. This is of interest to validate potential benefits of new irradiation strategies over conventional radiotherapy methods.

- [1] F. Sima, H. Kawano, A. Miyawaki, et al., ACS Applied Bio Materials. 2018, 1, 1667.
- [2] F. Jipa, S. Iosub, B. Calin, et al., Nanomaterials. 2018, 8, 583.
- [3] F. Sima, H. Kawano, M. Hirano, et al., Adv. Mater. Technol. 2020, 2000484.
- [4] C.E. Staicu, F. Jipa, I. Porosnicu, et al., App. Phys. A Mater. 2022, 128, 77.

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### COLL/HA Composite Materials as Drug-Delivery Systems in Bone Tissue Engineering

#### Mariana JIAN<sup>1-4</sup>, Denisa FICAI<sup>1,2,5</sup>, Viorel NACU<sup>4,6</sup>, Anton FICAI<sup>1-3,7,\*</sup>

- <sup>1</sup> Science and Engineering of Oxide Materials and Nanomaterials, Faculty of Applied Chemistry and Materials Science, National University of Science and Technology POLITEHNICA Bucharest, 011061 Bucharest, Romania
- <sup>2</sup> National Research Centre for Food Safety, National University of Science and Technology POLITEHNICA Bucharest, 060042 Bucharest, Romania;
- <sup>3</sup> National Centre for Micro and Nanomaterials, National University of Science and Technology POLITEHNICA Bucharest, 060042 Bucharest, Romania;
- <sup>4</sup> Laboratory of Tissue Engineering and Cell Cultures, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, MD-2004, Republic of Moldova
- <sup>5</sup> Department of Inorganic Chemistry, Physical Chemistry and Electrochemistry, Faculty of Applied Chemistry and Materials Science, National University of Science and Technology POLITEHNICA Bucharest, 011061 Bucharest, Romania.
- <sup>6</sup> Human Cells and Tissue Bank, Traumatology and Orthopedy Clinic Hospital, MD-2004, Republic of Moldova
- <sup>7</sup> Academy of Romanian Scientists, 050044 Bucharest, Romania
- \*anton.ficai@upb.ro

Bone is a remarkable composite material mainly based on Hydroxyapatite (HA) and Collagen (COLL). Considering this composition, many bone related grafts are based on such composite materials. Moreover, considering the various bone-related diseases a wide range of biological active agents are loaded in order to enhance or to induce new properties. The COLL/HA composite support is essential because bring osteoinductive and osteoconductive properties assuring a proper osteointegration but also resorption and can modulate the release of the biological active agents. Drug delivery systems (DDS) are usually designed for bone reconstruction and augmentation but also in the treatment of the fractures and other bone defects associated with various diseases including bone cancer, bone infections, osteoporosis, *etc.* These drug delivery systems were continuously improved and nowadays a wide range of drug delivery systems based on COLL/HA composite materials are known and even smart drug delivery systems were developed and proved to be efficient. These smart DDSs can be activated by specific internal or external stimuli such as pH, temperature, electromagnetic fields, *etc.*, and thus, even personalized treatment can be developed. The present work is mainly focused on presenting the challenges and the recent advances in the field of COLL/HA composite DDS used in the bone cancer treatment.

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## Design, Development and Characterisation of Smart Synthetic Bone Graft Materials for Advanced Therapies

# José M.F. FERREIRA<sup>1,2\*</sup>, Przemysław GOŁĘBIEWSKI<sup>1</sup>, Anuraag GADDAM<sup>2,3</sup>, Hugo R. FERNANDES<sup>2</sup>, Ryszard BUCZYNSKI<sup>1,4</sup>, Gregory TRICOT<sup>5</sup>, Hellmut ECKERT<sup>5,6</sup>, Adrian-Claudiu POPA<sup>7</sup>, George E. STAN<sup>7</sup>

- <sup>1</sup> Lukasiewicz Research Network Institute of Microelectronics and Photonics, 02–668 Warsaw, Poland
- <sup>2</sup> CICECO Aveiro Institute of Materials, Department of Materials and Ceramic Engineering, University of Aveiro, 3810-193 Aveiro, Portugal
- <sup>3</sup> Instituto de Física de São Carlos, Universidade de São Paulo, São Carlos, SP 13566-590, Brasil
- <sup>4</sup> Faculty of Physics, University of Warsaw, 02-093 Warsaw, Poland
- <sup>5</sup> LASIRE, UMR-CNRS 8516, Université de Lille, Villeneuve d'Ascq, France
- <sup>6</sup> Institut für Physikalische Chemie, Westfälische Wilhelms-Universität Münster, D-48149 Münster, Germany
- <sup>7</sup> National Institute of Materials Physics, 077125 Magurele, Romania
- \* jmf@ua.pt; jose.ferreira@imif.lukasiewicz.gov.pl

The common occurrence of bone defects and bone destruction caused by disease (osteoporosis, bacterial infections, osteoarthritis and tumour) or accidental factors (car accidents and trauma) have a huge impact on a patient's quality of life, and demand suitable grafting remediations [1]. Because of the limited availability of biological bone substitutes, several tissue engineering strategies have been widely considered in the reconstruction of vascularized bone tissue and in the treatment of bone defects, namely, the combination of cells, biological molecules and biomaterials [2]. The synthetic bone grafts might comprise different types of materials, including metals, ceramics, bioactive glasses, polymers and composites. They have to be judiciously selected according to the specific requirements of the bone substitutes in terms of the relevant physical, and functional properties. The close resemblance between the chemical composition of the inorganic part of the bone and hydroxyapatite (HA-Ca<sub>10</sub>(PO<sub>4</sub>)<sub>6</sub>(OH)<sub>2</sub>, almost bioinert) and tricalcium phosphate (TCP-Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>, resorbable) make them attractive to develop bone grafts based on calcium phosphates (HA, TCP, or biphasic compositions, pure and doped with therapeutic ions [3]. Moreover, bone tissue engineering strategies often involve the use of porous three-dimensional (3D) scaffolds that act as temporary supports and provide a suitable environment and architecture for bone regeneration and development [4]. A high and interconnected porosity with adequate pore sizes for allowing cell adhesion and proliferation, ensuring the diffusion of oxygen and nutrients to the cells and the removal of waste products are essential requirements. These requirements can be commonly achieved by using additive manufacturing [5], or by biomimetic approaches, such as transforming the aragonitic cuttlefish bone in the desired calcium phosphate composition, while preserving the highly porous and interconnected structure [6]. The first part of this presentation discloses the overall composition and, in particular, the surface chemistry of such scaffolds can be modified with special coatings for endowing them with specific functional properties such as enhanced bioactivity, drug storage and controlled in situ release. Bioactive glasses are other competitor materials for bone repair and regeneration [7]. Although the discovery of the first 45S5 Bioglass® has been regarded as a great breakthrough, its high alkali content causes serious shortcomings. In contrast, Alkali-free bioactive glasses [8] possess a set of highperforming biological key features [7,9]. Moreover, Alkali-free bioactive glass compositions inherently exhibit stable/metastable thermodynamic driven liquid-liquid phase separation (LLPS) that facilitates the sintering of the glass powders, being well suited for developing biomedical devices that depend on powder processing techniques. The first glass transition temperature is significantly lower than the crystallization onset temperature, providing a wide temperature window for controlling liquid state sintering [10]. On the other hand, LLPS negatively affects the fabrication of devices that involves glass shaping from the melt, such as fibre drawing [11]. This is because the second glass transition temperature is close to that of the onset of crystallization, thus leaving only a narrow temperature window for glass shaping.

The second part of this presentation is focused on the effects of NaBO<sub>2</sub> addition to a phase-separated Alkalifree bioactive glass composition (38.49 SiO<sub>2</sub> • 36.07 CaO • 19.24 MgO • 5.61 P<sub>2</sub>O<sub>5</sub> • 0.59 CaF<sub>2</sub>). Scanning electron microscopy reveals binodal phase separation involving two Si microphases with a droplet size of ~200 um. The local environments and spatial distribution of silicate, phosphate, and fluoride ions in this phaseseparated system were studied, using <sup>29</sup>Si, <sup>31</sup>P, <sup>11</sup>B, <sup>19</sup>F, <sup>25</sup>Mg, and <sup>23</sup>Na nuclear magnetic resonance (NMR) and infrared spectroscopy. The silicate units are dominantly of the metasilicate (Si<sup>2</sup> or  $Q_{2(Si)}$ ) type. The phosphate units exist mostly as orthophosphate (P<sup>0</sup> or Q<sub>0(P)</sub>) while the borate is present in the form of pyroborate (B<sup>1</sup> or T<sub>1(B)</sub>). Multinuclear dipolar re-coupling experiments indicate that the minority components F, P, and Na all occur within a common phase. Thus, atomic distribution scenarios involving the separation of these components into separate phases can be excluded. Based on the <sup>31</sup>P spin echo decay (SED) method along with Monte Carlo simulations analysis, the phosphate component forms clusters of sizes 1-4 nm, which are randomly embedded in an environment more dilute in phosphate. While <sup>19</sup>F SED results indicate that the fluoride ions do not form clusters and are close to randomly distributed, dipolar recoupling with 31P, using <sup>19</sup>F{<sup>31</sup>P} REDOR experiments, suggests a local environment resembling that of fluorapatite. Such local environment might be the reason behind the fast biomineralization rate of this type of bioactive glasses, All SBG compositions were subjected to cytocompatibility tests using human mesenchymal stem cell cultures (hMSCs). It was found that all SBGs elicited good biocompatibility, with some SBG formulations promoting hMSCs proliferation and differentiation, while others sustaining the stem cell phenotype. These findings prove that SBGs are a class of materials with immense potential for tailored bone grafting applications in future medicine.

- [1] R.S. Valtanen, Y.P. Yang, G.C. Gurtner, et al., Injury 2021, 52, S72–S77.
- [2] W. Wang, K.W.K. Yeung, Bioact. Mater. 2017, 2, 224–247.
- [3] S. Kannan, F.G. Neunhoefferb, J. Neubauerb, et al., J. Am. Ceram. Soc. 2008, 91, 1–12.
- [4] L. Roseti, V. Parisi, M. Petretta, et al., Mater. Sci. Eng. C. 2017, 78, 1246–1262.
- [5] S.M. Olhero; H.R. Fernandes, C.F. Marques, et al., J. Mat. Sci. 2017, 52, 12079–12088.
- [6] A.S. Neto, J.M.F. Ferreira, Materials 2018, 11, 1702.
- [7] H.R. Fernandes, A. Gaddam, A. Rebelo, et al., Materials 2018, 11, 2530.
- [8] A. Goel, S. Kapoor, R.R. Rajagopal, et al., Acta Biomater. 2012, 8, 361–372.
- [9] A.C. Popa, H.R. Fernandes, M. Necsulescu, et al., Ceram. Int. 2019, 45, 4368–4380.
- [10] A. Gaddam, G. Trico, P. Gołębiewski, et al., Acta Materialia, 2023, 259, 119203.
- [11] A. Gaddam, P. Gołębiewski, H.R. Fernandes, et al., J. Am. Ceram Soc., 2021, 104, 4492–4504.

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#### Evolution of Electrochemical Sensors from Macro to Nano

## Rasa PAULIUKAITE<sup>1\*</sup>, Justina GAIDUKEVIČ<sup>1</sup>, Justina STONYTĖ<sup>1</sup>, Vytautas ŽUTAUTAS<sup>1</sup>, Romualdas TRUSOVAS<sup>2</sup>

- <sup>1</sup>. Department of Nanoengineering, FTMC, LT-02300 Vilnius, Lithuania
- <sup>2</sup> Department of Laser Technology, FTMC, LT-02300 Vilnius, Lithuania \*pauliukaite@ftmc.lt

Chemical sensor development started in the middle of the  $20^{th}$  century. Over time, 20 years ago, they were combined into multisensors. Multisensors are divided into non-specific, *i.e.* qualitative (electronic noses or tongues) or specific, *i.e.* quantitative [1]. Electronic noses and tongues are already used in practice. However, it is not a challenging task to design quantitative sensors, since all the sensors have to be controlled by the same electronic system with different parameters for each sensor.

Initially, multisensors with the controlling part took up half a desk, while now they can be the size of a credit card due to micro- and nanotechnology. Electrochemical sensors are cost-effective and do not require complex sample preparation, especially if the samples are liquid. These sensors are relatively easy to miniaturise [1]. They are particularly necessary for personalised medicine.

Before complex multisensing systems or assays, individual miniaturised electrochemical sensors constructed of conductive polymers and carbon nanoparticles are first tested. Our group is developing microsensors for various analytes such as neurotransmitters (dopamine) [2], glucose [3], pH [4,5], Zn(II) and proteins (gliadin, wound-specific antibodies), *etc*.

- [1] R. Pauliukaite, E. Voitechovič, Sensors. 2020, 20, 3551.
- [2] J. Gaidukevic, R. Aukstakojyte, J. Barkauskas, et al., Appl. Surf. Sci. 2022, 592, 153257.
- [3] J. Gaidukevic, R. Aukstakojyte, M. Kozłowskic, et al., Electrochim. Acta. 2023, 446, 142113.
- [4] V. Žutautas, T. Jelinskas, R. Pauliukaite, J. Electroanal. Chem. 2022, 921, 116668.
- [5] V. Žutautas, R. Trusovas, A. Sartanavičius, et al., Chemosensors. 2023, 11, 329.

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#### Surface Modification for Label-free Sensing

#### Camelia BALA

Department of Analytical Chemistry, University of Bucharest, 030018 Bucharest, Romania camelia.bala@chimie.unibuc.ro

This lecture intends to be an overview of the research activity developed by our group in the sensing field, especially the design of the interface between the physical transducer and the biological recognition elements. The immobilization of the active biological component on the transducer surface represents a critical stage in the biosensor's development, and its goal is the settlement of the bioactive part on the surface of the physical transducer. The chosen immobilization procedure has to keep the biological component in the native conformation. On the other hand, the physical transducers should have an adequate sensitivity toward the species to be detected.

Recently, the World Anti-Doping Agency introduced in the Prohibited List the class of compounds "S2 - peptide hormones, growth factors, mimetics and related substances" the growth hormone secretagogue receptor analogues, ghrelin mimetics, which have the role of stimulating the natural hormone production, increase the muscle mass and reducing the percentage of adipose tissue. Athletes began using ghrelin (GH) agonists in order to gain an advantage over their opponents, based on the anabolic effects of growth hormone, risking both their sports careers and especially their health. In the present context, there is a high demand for rapid, accurate, specific methods for the detection of GH mimetics and the development of miniaturized and portable point-of-care devices for fast testing laboratories.

The lecture will illustrate the practical applications of surface modification of electrochemical and SAW sensors, focusing on layer-by-layer assembly and thiol-driven self-assembly and sol-gel chemistry, grafting chemistries including click chemistry and practical applications from environmental and biomedical analysis areas [1–4].

- [1] M. Puiu, V. Mirceski, C. Bala, Curr. Opin. Electrochem. 2021, 27, 100726.
- [2] M. Puiu, L.G. Zamfir, G.M. Danila, et al., Sensor, Actuat. B Chem. 2021, 345, 130416.
- [3] G.M. Danila, M. Puiu, L.G. Zamfir, et al., Talanta 2022, 237, 122905.
- [4] M. Puiu, O.-M. Istrate, V. Mirceski, et al., Anal. Chem. 2023, 95, 16185.

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## WIRELESS ELECTROCHEMISTRY: From Advanced Materials to (Bio)electroanalysis and Enantioselective Synthesis

#### Alexander KUHN

Univ. Bordeaux, CNRS, Bordeaux INP, F 33607 Pessac, France kuhn@enscbp.fr

Wireless electrochemistry, more scientifically also called bipolar electrochemistry, is a concept based on the fact that two opposite chemical processes, oxidation and reduction, occur simultaneously on the surface of a (semi)conducting object, without connection to a power supply [1]. We distinguish between exogenous bipolar systems, for which the primary driving force originates from an external electric field, and endogenous bipolar objects, where an asymmetric chemical composition provides the necessary thermodynamic power to induce spatially separated reactions [2]. The basic phenomena have already been described and used for a long time, but regained interest in recent years, because it became apparent that bipolar electrochemistry has attractive features for developing new applications in various areas. This is mostly due to several advantages over classic electrochemistry, such as the absence of an ohmic contact, the generation of a dual gradient of electroactivity on the same object and the possibility to address simultaneously thousands of objects. Also, some features of this type of electrochemistry allow performing experiments which simply cannot be done with a classic electrochemical set-up.

The objective of this presentation is to introduce first the basic aspects of bipolar electrochemistry, and then to illustrate some very recent applications of this concept studied in our group, ranging from materials science [3–6] and (bio)electroanalysis [7–10], to the generation of motion [11–16] and electrosynthesis [17,18], also of chiral molecules, thus opening interesting perspectives for the pharmaceutical industry [19,20].

- [1] L. Bouffier, D. Zigah, N. Sojic, A. Kuhn, *Bipolar electrochemistry*, in: Encyclopedia of Electrochemistry, Bard et al. (Eds.), Wiley, **2021**.
- [2] G. Salinas, L. Bouffier, N. Sojic, A. Kuhn, J. Solid State Electrochem. 2023 (in press).
- [3] A.A. Melvin, E. Lebraud, P. Garrigue, et al., Phys. Chem. Chem. Phys. 2020, 22, 22180.
- [4] S.M. Beladi-Mousavi, G. Salinas, N. Antonatos, et al., Carbon. 2022, 191, 439.
- [5] R. Gao, S. Mohsen Beladi-Mousavi, G. Salinas, et al., Nano Lett. 2023, 23, 8180.
- [6] P. Chassagne, P. Garrigue, A. Kuhn, *Adv. Mater.* **2023**, *36*, 2307539.
- [7] L. Zhang, B. Gupta, B. Goudeau, et al., J. Am. Chem. Soc. 2018, 140, 15501.
- [8] S. Assavapanumat, B. Gupta, G. Salinas, et al., Chem. Comm. 2019, 55, 10956.
- [9] S. Arnaboldi, B. Gupta, T. Benincori, et al., Anal. Chem. 2020, 92, 10042
- [10] S. Arnaboldi, G. Salinas, A. Karajic, et al., Nat. Chem. 2021, 13, 1241.
- [11] B. Gupta, L. Zhang, A.A. Melvin, et al., Chem. Sci. 2021, 12, 2071.
- [12] A. A. Melvin, B. Gupta, K. Tieriekhov, et al., Adv. Funct. Mater. 2021, 31, 2101171.
- [13] G. Salinas, A.L. Dauphin, C. Colin, et al., Angew. Chem. Int. Ed. 2020, 59, 7508.
- [14] G. Salinas, A.L. Dauphin, S. Voci, et al., Chem. Sci. 2020, 11, 7438.
- [15] I.-A. Pavel, G. Salinas, A. Perro, et al., Adv. Intell. Syst. 2021, 3, 2000217.
- [16] G. Salinas, K. Tieriekhov, P. Garrigue, et al., J. Am. Chem. Soc. 2021, 143, 12708.
- [17] C. Zhang, H. Zhang, J. Pi, et al., Angew. Chem. Int. Ed. 2022, 61, e202111804.
- [18] M. Ketkaew, S. Assavapanumat, S. Klinyod, et al., Chem. Comm. 2022, 58, 4312.
- [19] G. Salinas, S. Arnaboldi, P. Garrigue, et al., Faraday Discuss. 2023, 247, 34.
- [20] S. Arnaboldi, G. Salinas, G. Bonetti, et al., Angew. Chem. Int. Ed. 2022, 61, e202209098.

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## Development of Innovative Nano-Systems for the Targeted Treatment of Cancer

### Alexandra PUSTA<sup>1</sup>, Mihaela TERTIŞ<sup>1</sup>, Rodica TURCU<sup>2</sup>, Victor DICULESCU<sup>3</sup>, Cecilia CRISTEA<sup>1,\*</sup>

- <sup>1</sup> Department of Analytical Chemistry, Iuliu Haţieganu University of Medicine and Pharmacy, 400349 Cluj-Napoca, Romania
- <sup>2</sup> National Institute for Research and Development of Isotopic and Molecular Technologies, 400293 Cluj-Napoca, Romania
- <sup>3</sup> National Institute of Materials Physics, 077125 Magurele, Romania
- \*ccristea@umfcluj.ro

Chemotherapy represents the mainstay of treatment for a wide variety of cancers that cannot benefit from surgical procedures. Despite its efficiency, chemotherapy presents many drawbacks such as systemic side effects and lack of specificity for tumour tissue. For this reason, it is crucial to develop novel methods that can ensure the targeted delivery of the active compound to the tumour site. This can be achieved using two different strategies: passive transport, which relies on the specific properties of the tumour tissue, or active transport, in which delivery systems are functionalized with structures that show specificity towards tumour tissues (antibodies, enzymes, aptamers) [1].

The present work proposes four different nano-systems for the targeted delivery of several chemotherapeutics: nanosomes loaded with (i) doxorubicin and (ii) carboplatin for passive delivery and magnetic (iii) nanoparticles or (iv) nanoclusters for the active delivery of sorafenib.

In the case of passive approaches, the nanosomes were incubated with the corresponding drug solutions and drug loading was confirmed by UV-Vis spectrophotometry. Subsequently, drug release was carried out in media of different pH values and the maximum release was obtained in acidic pH for both chemotherapeutics. This represents an advantage, as the pH of the tumour microenvironment is more acidic compared to that of healthy tissues [2]. To evaluate the release of doxorubicin and carboplatin from the nano-systems, electrochemical methods were developed for the detection of these substances. Direct electrochemical detection was performed on bare in-house produced electrodes in the case of carboplatin and on in-house produced electrodes modified with gold nanostructures in the case of doxorubicin. The results obtained were compared to those obtained by UV-Vis spectrophotometry and good correlations were observed. A schematic representation of the protocol used for the development and testing of doxorubicin-loaded nanosomes is represented in Fig. 1.

In the case of active delivery, two types of magnetic nano-carriers were used: azelaic acid functionalized magnetic nanoparticles and poly-tartaric acid functionalized magnetic nanoclusters.

Aptamer TLS11a, a DNA aptamer with high affinity for hepatocellular carcinoma HepG2 cells, was used for the functionalization of the magnetic carriers. The functionalization was performed in two steps: first, the carboxyl groups on the surface of the nano-carriers were activated using a mixture of N-hydroxysuccinimide and 1-ethyl-3-(3-dimethylaminopropyl)carbod iimide and next, the amino-terminated aptamer was added. This ensured the formation of an amidic bond between the amino group in the aptamer structure and the activated carboxyl groups. Aptamer functionalization was confirmed using UV-Vis spectrophotometry and electrochemical impedance spectroscopy in the case of magnetic nanoparticles. The next step consisted in loading sorafenib onto the modified magnetic nano-carriers and performing sorafenib release studies in buffers of different pH values. Both steps were confirmed using UV-Vis spectrophotometry and a better release profile was observed at pH 5.5 compared to pH 7.4. A schematic representation of each step in the development of the magnetic nano-carriers is represented in Fig. 2.

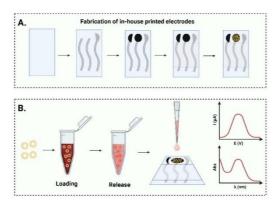


Fig. 1. Schematic representation of the protocol used for the development and testing of doxorubicin-loaded nanosomes.

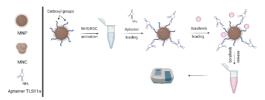


Fig. 2. Schematic representation of the development of aptamer modified, sorafenib loaded magnetic nanocarriers.

Cell internalization tests were performed in the case of magnetic nanoparticles on two different cell lines: HepG2 hepatocellular carcinoma cells and fibroblasts. A higher internalization in HepG2 cells was observed in the case of aptamer-modified nanoparticles compared to unmodified nanoparticles at all concentrations tested. In the case of fibroblasts, the presence of the aptamer led to lower internalizations at all concentrations. These results demonstrate the positive impact of the aptamer functionalization on the specificity of the nanocarriers for tumour cells. An electrochemical method for the detection of sorafenib was also developed based on commercially available screen-printed electrodes. The electrochemical detection of sorafenib was used to determine the drug loading and good correlations with the control UV-Vis method were observed. The limit of detection of the developed method did not allow the quantification of sorafenib from release studies.

In conclusion, drug delivery systems for the passive transport of doxorubicin and carboplatin and active transport of sorafenib have been successfully developed. Their characterization was carried out using spectral methods as well as electrochemical methods. All carriers demonstrated better drug release profiles at acidic pH compared to neutral pH, which represents an advantage for cancer therapy. Moreover, in the case of active delivery, it was demonstrated that the aptamer functionalization increases the internalization of drug carriers in tumour cells, while decreasing the internalization in healthy cells. Direct electrochemical detection was performed for all three chemotherapeutics and applied in loading and release studies in the case of doxorubicin and carboplatin and for loading studies in the case of sorafenib, demonstrating the applicability of electrochemical methods in the development of pharmaceutical formulations.

- [1] M.F. Attia, N. Anton, J. Wallyn, et al., J. Pharm. Pharmacol., 2019, 71 1185.
- [2] A. Pusta, M. Tertis, I. Crăciunescu, et al., Pharmaceutics, 2023, 15, 15071872.

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# Paper-based Printed Electrochemical (bio)sensors as Smart and Sustainable Point-of-Care Devices

#### Fabiana ARDUINI

Department of Chemical Science and Technologies, University of Rome "Tor Vergata", Rome, Italy fabiana.arduini@uniroma2.it

As reported in my recent review entitled "Electrochemical paper-based devices: When the simple replacement of the support to print ecodesigned electrodes radically improves the features of the electrochemical devices" published in Current Opinion in Electrochemistry SI: Emerging Opinions (2022) [1]: "Paper-based electrochemical (bio)sensors have emerged as highly attractive analytical devices for their superior sustainable features, such as avoiding the use of polyester as support and the reduction of waste, being incinerated after use. However, paper-based electrochemical (bio)sensors have recently demonstrated further advantages, including the simple combination with vertical microfluidics and their use as a reservoir to deliver smart electrochemical (bio)sensors able to (i) contain the reagents; (ii) preconcentrate the target analyte, and iii) synthesize the nanomaterials inside the paper network. Furthermore, these devices have demonstrated their ability to overcome the limitations of the other printed electrochemical sensors in the measurement of entirely liquid samples by detecting the target analyte in the aerosol phase or solid sample, without the additional sampling system. These achievements highlight their valuable and varied advantages in the sensing sector". In this plenary lecture, I will report on the roadmap research activity carried out in the last 8 years related to the development of paper-based electrochemical devices for delivering lab-on-a-chip on paper as well as sustainable tools for overcoming the limitation of polyester-ceramic based printed sensors [2–9]. Furthermore, following the approach recently selected for printed electronics in which the hybrid systems have been the most useful for market entry, we recently demonstrated this approach for a market entry device for virus detection in saliva (patent filled), a wearable paper-based immunosensor washing-free for cortisol detection in sweat [10], and a paper-based device combined with polyvinyl chloride electrochemical system in which a paper layer loaded with reagents is inserted into this device, working as a new concept of paper card-like for a reagent-free and easy measurement of target analyte (i.e., glucose) in solution (i.e., tears) [11].

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- [1] F. Arduini. Curr. Opin. Electrochem. 2022, 35, 101090.
- [2] S. Cinti, D. Talarico, G. Palleschi, et al., Anal. Chim. Acta 2016, 919, 78-84.
- [3] S. Cinti, C. Minotti, D. Moscone, et al., Biosens. Bioelectron. 2017, 93, 46-51.
- [4] G. Scordo, D. Moscone, G. Palleschi, et al., Sens. Actuat. B 2018, 258, 1015–1021.
- [5] S. Cinti, D. Moscone, F. Arduini, et al., Nat. Protoc. 2019, 14, 2437–2451.
- [6] N. Colozza, K. Kehe, G. Dionisi, et al., Biosens. Bioelectron. 2019, 129, 15–23.
- [7] V. Caratelli, A. Ciampaglia, J. Guiducci, et al., Biosens. Bioelectron. 2020, 165, 112411.
- [8] N. Colozza, S. Tazzioli, A. Sassolini, et al., Anal. Chem. 2021, 93, 14369–14374.
- [9] V. Caratelli, E. Di Meo, N. Colozza, et al., J. Mater. Chem. B. 2022, 10, 9021–9039.
- [10] L. Fiore, V. Mazzaracchio, A. Serani, et al., Sens. Actuat. B 2023, 379, 133258.
- [11] L. Fiore, A. Sinha, N. Seddaoui, et al., Chem. Comm. 2023, 59, 4300.

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## Improving the Mechanical Performance of Bioceramic Scaffolds for Biomedical Applications

## Antonia PAJARES\*, F. MARTÍNEZ-VÁZQUEZ, A. MOTEALLEH, S. EQTESADI, F.H. PERERA, P.MIRANDA

Departamento de Ingeniería Mecánica, Energética y de los Materiales, Universidad de Extremadura, 06006 Badajoz, Spain

\*apajares@unex.es

The optimal approach to address the problems associated with the repair of bone-related lesions is to develop artificial biomaterials, with bone-like mechanical properties (low density and stiffness and high strength and toughness) and able to interact with the tissues, so that they can actively induce bone regeneration. A strategy to achieve this type of interaction with surrounding tissue and to stimulate cell penetration and proliferation after implantation is to use porous matrices of osteophilic materials, such as bioceramics (HA, TCP) and bioglasses (45S5, 13-93). The porosity of this structures must be interconnected and with a certain interconnection size, to allow vascularization, cell penetration and nutrient diffusion into the scaffold. In conventional porous scaffold fabrication methods (solvent casting, fibre meshing, gas foaming, melt moulding, freeze drying, *etc*) it is difficult to precisely control pore size, geometry, and spatial distribution, and therefore to achieve the required degree of interconnectivity it is necessary to produce very high porosities, which translate into very low strengths that severely limits the range of applications. To overcome this hurdle, three different strategies are investigated in this study.

Optimizing the scaffold macropore architecture using robocasting as the fabrication method. This technique, also known as direct ink writing, consists of the robotic deposition of highly concentrated colloidal suspensions (inks) capable of fully supporting their own weight during assembly thanks to their carefully tailored composition and rheological properties. Thus, a 3D structure is printed directly as a network of ink rods extruded through a deposition nozzle of certain diameter mounted on a 3-axis motion stage, controlled independently by a computer-aided direct-write program. The high level of control over pore architecture provided by robocasting makes possible to achieve the required degree of pore interconnectivity with relatively low porosities, which improves significantly the mechanical properties of the scaffolds.

Improving the intrinsic strength and toughness of the individual bars composing the scaffold. Since rod microporosity reduces the intrinsic mechanical properties of the rods (the micropores act as starting flaws for cracking) dense, defect free struts are desirable. This can be achieved through optimization sintering and densification and/or through the incorporation of a reinforcing agent (e.g., graphene-based nanoplatelets) to the bioceramic microstructure.

Adding a biodegradable polymeric phase. Despite the improvement in pore architecture achieved by robocasting and in the intrinsic properties of the individual bars, the main limitation of these ceramic scaffolds still lies in their intrinsic brittleness and the poor mechanical resistance associated to their porosity. Infiltrating the bioceramic scaffold with biodegradable polymers to obtain either fully-impregnated structures or coated structures improves the scaffold's mechanical performance, both in terms of strength, due to defect healing and stress shielding mechanisms; and toughness, as a consequence of a crack bridging mechanism produced by polymer fibrils.

To quantify the mechanical enhancement attained through these approaches, the mechanical performance of the developed materials is evaluated under compressive and bending stresses. The obtained results are compared with values reported in the literature for bone tissue and their implications concerning the use of bioceramic robocasted scaffolds in load-bearing bone tissue engineering applications are discussed.

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# Leveraging the High Resolution of Digital Light Processing in the Additive Manufacturing of High-Performance Composites for Biomedical Applications

## Pedro MIRANDA\*, C. PAREDES, F.J. MARTÍNEZ-VÁZQUEZ, S. MORENO-MARTÍNEZ, S. BAYÁN, Antonia PAJARES

Departamento de Ingeniería Mecánica, Energética y de los Materiales, Universidad de Extremadura, Avda de Elvas s/n, 06006 Badajoz, Spain

This work describes innovative manufacturing technologies that leverage the high resolution of fotocuring additive manufacturing techniques such as Digital Light Processing (DLP) for the production of bioinspired ceramic-polymer hybrid materials with enhanced mechanical performance. These high-performance composites find application, among other fields, in bone tissue engineering scaffolds, dental prosthesis and other biomedical implants.

Additive Manufacturing (AM) techniques have been widely used to fabricate porous substrates for biomedical applications. Developing AM scaffolds from materials with bonelike properties that are capable to interact with the tissues and actively induce bone regeneration has permitted overcoming the main issues of currently available procedures for repairing large bone lesions, namely: the limited amount of material and need of secondary surgical sites in the case of autografts, the risk of immunogenic response and disease transmission from donor in the case of allografts, and the fixation problems of current bioinert prostheses. However, pure bioceramic scaffolds are mechanically weak and very brittle, which prevents their widespread use in the repair of bone defects in load-bearing regions of the skeleton. In this work, digital light processing (DLP) is used to obtain composite scaffolds with controlled microstructure, pore architecture and optimal mechanical performance. Concentrated  $\beta$ -tricalcium phosphate (TCP) inks are used to produce porous structures consisting of a tetragonal three-dimensional mesh of interpenetrating hollow tubes that were subsequently impregnated by a polymeric phase to obtain core/shell composite struts. This particular strut architecture offers a promising strategy to optimize the mechanical performance in terms strength, and especially of toughness, of the scaffolds without jeopardizing their bioactivity and osteoregenerative properties.

Ongoing progress towards the additive fabrication of novel ceramic/polymer bioinspired composites with a microstructure mimicking that of the enamel in human teeth are also discussed. Intricate columnar ceramic preforms with intercolumn gaps resembling the convoluted hydroxyapatite-rich rods found in natural enamel can be produced either through direct DLP printing of bioceramic photocurable suspensions or through indirect DLP strategies were a sacrificial negative resin mould is fabricated by DLP. In the latter case, the ceramic preform is produced by casting a highly concentrated ceramic slurry into the mould, which is subsequently eliminated in a heat treatment before sintering the ceramic particles and consolidating the preform. In either case, to obtain the desired bioinspired composites, the ceramic preform is infiltrated by a ductile polymer to mimic the inter-rod sheath in natural enamel. In this way, highly damage-tolerant and wear resistant hybrid biomaterials can be formed. The developed materials will significantly improve the effectiveness and durability of dental restorations over existing commercial alternatives, thus helping to reduce the need for replacement interventions with their associated cost and risk for the patient.

The new bioinspired composites and the novel manufacturing processes described in this work may become essential enabling technologies for the realization of bioinspired high-performance composites, that could not only revolutionize the biomaterials industry, but have a dramatic impact in other industrial applications too.

**Acknowledgments:** This work has been funded through grant PID2021-123218OB-I00 by MCIN/AEI /10.13039/501100011033 and ERDF A way of making Europe.

<sup>\*</sup>pmiranda@unex.es

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## Nano-Biomaterials' Interactions with Cells: Challenges and Opportunities

#### Mihaela G. MOISESCU

Biophysics and Cellular Biotechnology Department, Excellence Center for Research in Biophysics and Cellular Biotechnology, Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, 050474 Bucharest, Romania

mihaela.moisescu@umfcd.ro

Development and engineering of nanomaterials (NMs) for efficient therapy of various pathologies (e.g., cancer) know an extensive progress over the last two decades with special attention given to modulating the material properties through synthesis processes (e.g., chemical structure, size, area, pore volume, chemical groups attached to the surface, etc) aiming to improve targeting and drug delivery. Another key point is a deeper knowledge of materials effects on living cells by NMs accurate tracking from membrane penetration to NMs final intracellular destination. Various NMs physico-chemical parameters as well as the type and biological features of the cell influence the intracellular fate of the nanomaterial. Thereupon several cell-based, including label-free technologies got an increasing attention in the preclinical NMs-based drug delivery studies.

During the talk, it will be presented our group's experience in evaluating the effects of several categories of NMs carrying cytotoxic molecules (*e.g.*, irinotecan) and under various functionalization (*e.g.*, folate, fucoidan) on cells in culture (*e.g.*, murine fibroblasts, human colonic adenocarcinoma cells). Results obtained using endpoint tests (like formazan-based colorimetric tests, comet assay for DNA) as well as real-time label-free evaluation of cell growth (like impedance-based cell technique) will be discussed for different nanoparticles in terms of chemical structure (like mesoporous silica, zinc oxide) or molecules modifying the cellular processes involved in the NMs incorporation (like inhibitors of endocytosis).

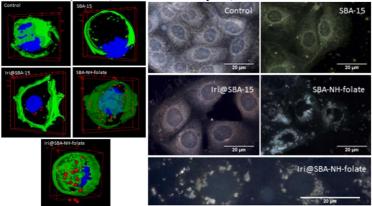


Fig. 1. Caco-2 cells incubated 24h with SBA-15 mesoporous silica nanoparticles functionalized with folate and loaded with irinotecan [1]. (left) 3D reconstructions of cells (cytoplasm green, nuclear DNA blue and nanoparticles red). Green zone appears discontinuous for visualization purposes.

(right) Hyperspectral images of cells where the intracellular accumulations of nanoparticles can be seen as bright spots.

A combination of visualization techniques implying fluorescence, hyperspectral and enhanced dark field microscopy was used to quantitatively evaluate the penetration and localization of NMs within a cell.

A methodology for processing serial Z-stacks of fluorescent and dark field images was developed to obtain 3D cell images [2]. Then, the nanomaterials concentrations (zinc oxide or SBA-15 nanoparticles) were

calculated in 3D reconstructions of cellular compartments like nucleus, cytoplasm, shells adjacent to nucleus or membrane.

Moreover, by hyperspectral microscopy not-labelled NMs were intracellularly found, counted, and tracked in correlation with their spectral signature

A preferential accumulation of NMs in the close vicinity of specific cell structures will be presented and the advantages and limitations of these combined techniques will be discussed. It will be shown that the cytotoxic effects of some drugs were enhanced when delivered by NMs compared to administration in homogeneous solution.

- [1] L.C. Miclea, M. Mihailescu, N. Tarba, et al., Nanoscale, 2022, 14, 12744.
- [2] M. Mihailescu, L.C. Miclea, A.M. Pleava, et al., Biomed. Opt. Express, 2023, 14, 2796–2810.

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# Composites based on Biopolymers-Bioactive Glasses/Glass-ceramics containing Cu and Au for Tissue Engineering Applications

#### Klára MAGYARI<sup>1,2</sup> and Lucian BAIA<sup>1,2,3,\*</sup>

- <sup>1</sup> Interdisciplinary Research Institute on Bio-Nano-Sciences, Babeş-Bolyai University, Cluj-Napoca, Romania
  <sup>2</sup> Institute for Research-Development-Innovation in Applied Natural Sciences, Babeş-Bolyai University, Cluj-Napoca, Romania
- <sup>3</sup> Faculty of Physics, Babes-Bolyai University, Cluj-Napoca, Romania
- \*lucian.baia@ubbcluj.ro

An excellent scaffold should be designed to simulate the natural mechanism of regeneration from the human body, and therefore, to obtain such a scaffold, the following requirements should be fulfilled: excellent bioactivity, good biocompatibility, osteoconductivity, osteoinductivity, simulate angiogenesis, relevant structural-mechanical properties, and biodegradable properties [1]. A promising approach for solving several mentioned issues is the use of composites with polymer, ceramics, metals, cells, and growth factors [2]. Particularly, alginate (Alg) and pullulan (Pll) were widely used as biomaterials for bone tissue engineering [3], while bioactive glasses and glass-ceramics (GC) with gold nanoparticles (AuNPs) were found to stimulate keratinocyte cell proliferation [4]. On the other hand, the use of CuO is justified by the improvement of the cell viability and angiogenesis properties as well as a good antibacterial effect [5].

Taking into consideration above mentioned aspects, our research group developed and investigated a series of novel composites based on a bioactive matrix (i.e., silicate glasses or GC), and biopolymers like Alg, Pll) containing CuO or differently shaped AuNPs by assessing their bioactive, biocompatible, and antibacterial properties. Our first interest was to combine Cu containing bioactive GC-based composites with Alg and Pll natural polymers for the synthesis of new biocompatible hydrogels and their use as support for in vivo tissue regeneration with antibacterial properties. In the beginning, it was shown that bioactive GC with relatively small amounts of CuO (i.e., 0.5 and 1.5 mol%) have excellent cell viability and good antibacterial effect against Staphylococcus aureus. Further, evaluating the bone regeneration response of these Alg-Pll-GC composite scaffolds in an experimental long bone defect orthotopically implant it proved a very good in vivo quality, in terms of bone regeneration and osteogenic properties. Other studies demonstrated that Alg-Pll-bioactive glasses with gold nanoparticles (Alg-Pll-BGAuSP) are promising materials for soft and bone engineering endeavors [6]. The composites, including the control sample containing β-tricalcium phosphatehydroxyapatite (β-TCP/HA), were implanted in bone defect in Wistar rats for 8 weeks, after that the remained materials were recovered. Based on the in vivo subcutaneous analyses the polymer composites with BGAuNP have shown excellent biocompatibility at 14, 30, and 60 days, exhibiting marked angiogenesis while, tissue proliferation was confirmed by a high number of Vimentin-positive cells, in comparison with the polymer composite that contains \( \beta \text{TCP/HA} \), which induced an inflammatory response represented by a foreign body reaction. The obtained results indicated that the presented composites can be real promising candidates for use in future tissue engineering applications.

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- [1] S. Wu, X. Liu, K.W.K. Yeung, et al., Mater. Sci. Eng. R Rep. 2014, 80, 1–36.
- J. Venkatesan, I. Bhatnagar, P. Manivasagan, et al., Int. J. Biol. Macromol. 2015, 72, 269–281.
- [3] R.P. Babu, K. O'Connor, R. Seeram, *Prog. Biomater.* **2013**, 2, 1–16.
- [4] K. Magyari, T. Nagy-Simon, A. Vulpoi, et al., Mater. Sci. Eng. C 2017, 76, 752–759.
- [5] R.A. Popescu, K. Magyari, A. Vulpoi, et al., Biomater. Sci. 2016, 4, 1252–1265.
- [6] A. Dreanca, M. Moresan-Pop, M. Taulescu, et al., Mater. Sci. Eng. C 2021, 123, 112006.

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## Steering Biological Processes to Stimulate Bone Formation

#### Jeroen van den BEUCKEN

Section of Regenerative Biomaterials, Department of Dentistry, Radboud University Nijmegen Medical Center, Radboudumc, Nijmegen, the Netherlands jeroen.vandenbeucken@radboudumc.nl

Bone formation is a physiological process required during embryogenesis, skeletal growth, skeletal remodelling, and bone healing following trauma. The latter often requires surgical intervention to fill bone voids and/or stabilize bone fractures. Increasingly frequently, such interventions include the installation of biomaterials, which need to perform in a reliable and effective manner. For bone substitute materials, this means that the biomaterial should interact with bone tissue to heal a bone defect within a limited time frame. The biological performance of biomaterial-based bone substitute materials relates to bioactivity, osteoconductivity, and osteoinductivity. Bioactivity is the biomaterial property that refers to the possibility to achieve direct bone binding and apposition. Osteoconductivity extends on this by allowing growth of bone tissue along a biomaterial surface. Finally, osteoinductivity is the property that a biomaterial can induce *de novo* bone formation. It is important to emphasize that the gold standard in bone substitution is autologous bone, which possesses all these three performance criteria. Biomaterials developed for the purpose of bone substitution generally are bioactive and osteoconductive, but lack osteoinductive properties.

Biomaterial-based bone substitution has predominantly focused on the development of calcium phosphates (CaPs). An often-used justification for their (clinical) success is the fact that CaP in the form of hydroxyapatite is the mineral component of bone extracellular matrix. However, the true value of CaPs for bone substitution lies in their bioactive and osteoconductive properties and the options to render CaPs gradually degradable. Recently, few reports on osteoinductive properties of CaPs have been published, but the mechanism by which osteoinduction works remains elusive. In this presentation, the cellular basis for osteoinduction is reviewed and focus is placed on those biomaterial surface properties that stimulate *de novo* bone formation.

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## Biocomposites Based on Functionalized Mesoporous Silica

Daniela BERGER<sup>1,\*</sup>, Mihaela DEACONU<sup>1</sup>, Simona IONIȚĂ<sup>1</sup>, Ana-Maria BREZOIU<sup>1</sup>, Ana-Maria PRELIPCEAN<sup>2</sup>, Roxana-Cristina POPESCU<sup>3</sup>, Cristian MATEI<sup>1</sup>, Mona MIHĂILESCU<sup>4</sup>, Diana-Iulia SAVU<sup>3</sup>

- <sup>1</sup> Faculty of Chemical Engineering and Biotechnologies, National University of Science and Technology POLITEHNICA Bucharest, 011061 Bucharest, Romania
- <sup>2</sup> National Institute of R&D for Biological Sciences, 060031 Bucharest, Romania
- <sup>3</sup> Holographic Imaging and Processing Laboratory, Centre for Research in Fundamental Sciences Applied in Engineering, National University of Science and Technology POLITEHNICA Bucharest, 060042 Bucharest, Romania,
- <sup>4</sup> Department of Life and Environmental Sciences, "Horia Hulubei" National Institute for Research and Development in Physics and Nuclear Engineering, 077125 Magurele, Romania
  <a href="mailto:\*\*daniela.berger@upb.ro">\*daniela.berger@upb.ro</a>

Development of new treatments by combining therapies or the design of efficient targeted drug delivery systems represents a hot topic of research for human health [1]. Mesoporous silica nanoparticles (MSN) are widely used as carriers for many biological substances not only due to their ability to host organic molecules, but also because of the possibility to modulate their surface properties [2] by attaching either organic moieties or inorganic nanoparticles.

In this regard, we develop new targeted co-delivery systems of doxorubicin (Dox) and resveratrol (Resv) based on MSN functionalized with phenylboronic acid moieties (MSN-BA). Boronic acid groups are able to interact with various molecular targets, enzymes, receptors, nucleic acids etc. and can bind on sialic acid groups of cancer-associated mucin-1 protein [3]. The developed drug delivery systems were characterized by various techniques such as wide-angle X-ray diffraction that evidenced the presence of organic molecules in amorphous state into silica mesopores, FTIR spectroscopy, which emphasized strong interactions between doxorubicin and carrier, thermal analysis (DTA-TG) that was used to quntify the amount of active pharmaceutical ingredients in drug delivery systems. Doxorubicin and resveratrol release profiles were determined in phophate buffer solution pH 5.5 and respective pH 7.4. If Dox,Resv@MCM-BA is compared with Dox@MCM-BA, the presence of resveratrol in the drug delivery system caused a faster release kinetics of the cytostatic agent, as well as a higher cumulative doxorubicin release after 24 h. The cytotoxicity of developed drug delivery systems was assessed on BJ fibroblast dermal cells and BT474 breast cancer cell line. The results revealed an enhanced antiproliferative effect when resveratrol was present as co-delivery drug besides doxorubicin. For both systems the cytotoxic effects on BJ cells in culture was lower than on BT474 cells. Hyperspectral imaging was used to investigate interactions between nanoparticles and the two mentioned cell-types to observe their preferential accumulation inside cells. A higher amount of Dox@MCM-BA nanoparticles BT474 cells than in the case of BJ fibroblasts was noticed.

Many efforts are focused on developing new composite materials based on phytocompounds as antibacterial agents for replacement of antibiotics or as anti-inflammatory agents. In this context, we obtained polyphenolic extracts from wild berry leaves that were further encapsulated into MSN functionalized with organic groups or modified with ZnO or Ag to enhance their stability over time. The properties of extracts were evaluated before and after encapsulation into functionalized MSN. Generally, the results showed improved properties for encapsulated extracts than for the corresponding free extracts. For instance, quantification of TNF- $\alpha$  cytokines showed that the wild bilberry leaves extract encapsulated in hollow mesoporous silica modified with ZnO (HS ZnO) provided a better anti-inflammatory activity than that of the free extract. The composite

containing HS ZnO showed a synergistic antibacterial activity due to both extract and ZnO nanoparticles attached to silica surface. We developed biocomposites by including encapsulated extract in mesoporous silica into colaggen matrix [4].

Acknowledgement: The financial support from UEFISCDI through projects PCE no. 117/2022 and 576PED/2022 is highly appreciated.

- [1] S. Tran, P.J. De Giovanni, B. Piel, et al., Clin. Transl. Med. 2017, 6, 44.
- [2] H. Ahmed, S. Sudhakar Gomte, E. Prathyusha, et al., J. Drug Delivery Sci. Technol., 2022, 76, 103729.
- [3] X. Zhang, S. Zhang, S.J. Baek, et al., ChemBioChem. 2017, 18, 1578.
- [4] M. Deaconu, A.M. Prelipcean, A.M. Brezoiu, et al., Pharmaceutics 2023, 15, 312.

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## Nanomaterials for Health Science Applications

#### Stefano BELLUCCI

INFN-Laboratori Nazionali di Frascati, 00044 Frascati, Italy bellucci@lnf.infn.it

We review recent progresses on applications of nanostructured materials to biology and medicine, ranging from biosensors devices to functionalized nanoparticles and nanocomposites for drug delivery. We pay special attention to the fields of neurodegenerative diseases and in general to the brain. We also consider the potential dangers related to the utilization of engineered nanomaterials, both for the professionally exposed workers and the general public exposure to commercially available products based on nanomaterials.

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## Raman and SERS Investigations on Pharmaceuticals

#### Monica BAIA<sup>1,2</sup>

- <sup>1</sup> Faculty of Physics, Babes-Bolyai University, 400084 Cluj-Napoca, Romania
- <sup>2</sup> Institute for Research-Development-Innovation in Applied Natural Sciences, Babeş-Bolyai University, 400294 Cluj-Napoca, Romania

#### monica.baia@ubbcluj.ro

Today, the focus of medicine is on individualized diagnosis and treatment of patients. Although this path is still in its beginning, every small step in this direction will be a big step towards achieving this goal. To understand the behaviour of a molecule in various interactions in different environments, a complete analysis of its chemical and physical properties is required. Vibrational spectroscopic methods (Raman and FT-IR) combined with density functional theory (DFT) calculations are perfect tools for this purpose [1]. However, in some cases, weak Raman signal intensity and fluorescence interference make the use of Raman spectroscopy impossible. Surface-enhanced Raman spectroscopy (SERS) offers a possibility to overcome these drawbacks; it allows the detection of molecules at very low concentrations [2] due to the amplification of the Raman signal of species adsorbed on a metal surface. SERS spectroscopy is also used to understand the action of drugs as it is essential to identify any alteration of the adsorbed species structure relative to that of the free molecule. In these trials, the metal surface can serve as a mimic of a biological interface and, after elucidating the mechanism of adsorption of a molecule on this surface, the study can be extended to adsorption on membranes or other biological surfaces of interest for therapeutic treatments to imitate the adsorption of drugs occurring into the organism. Moreover, due to its high sensitivity and ability to detect analytes at low concentrations, SERS is an appropriate technique in therapeutic drug monitoring that could help physicians to use the optimal dose to achieve a more effective treatment tailored for each patient [3]. Taking into consideration the above-mentioned aspects we carried out in our group detailed vibrational investigations by means of FT-IR and Raman techniques coupled with DFT calculations on different pharmaceuticals such as anti-inflammatory drugs, antibiotics, tranquilizers and sedatives, chemotherapeutics, etc. to provide insights into their structure [4]. Furthermore, by analysing the SERS spectra, the adsorption behaviour i.e. chemisorption or physisorption, the adsorption site, the orientation of the adsorbed drug molecules on the noble metal surface, was elucidated. The influence of different factors such as pH value and concentration were investigated, and the lowest detectable concentration was also established. Despite its established sensitivity, SERS applied to quantitative analysis is still very challenging. To make the step towards clinical applications, it is necessary to obtain the same results regardless of location, equipment, or user and interlaboratory studies are currently the best way to achieve this. A recent study [5] involving 15 laboratories, including ours, was aimed to assess the reproducibility and trueness of a quantitative SERS method and to compare different methods. The study suggested that SERS is a method which can be consistently used by different laboratories if it is very well-defined. The tested methods produced a range of reproducibility results, but the best ones were reasonably reproducible, with an average standard error of performance as low as 12% and 13%. The obtained results were encouraging since different instruments were used over a wide time frame, with different setup and acquisition parameters. The next step should be the evaluation of each source of experimental uncertainty (e.g., substrates, instruments, and operators) for the best performing methods. Nevertheless, it is obvious that Raman and SERS are promising tools to be used in medical applications such as therapeutic drug monitoring or personalized medicine.

- [1] J. Ren. S.J. Mao, J.D. Lin, et al., Curr. Pharma. Design 2022, 28, 1445–1456.
- [2] E.L. Ru, P. Etchegoin, *Principles of Surface-Enhanced Raman Spectroscopy and Related Plasmonic Effects*, Elsevier, New Zealand, 2009.
- [3] C. Liu, S. Weber, R. Peng, et al., TrAC Trends in Analytical Chemistry 2023, 164, 117094.
- [4] M. Baia, S. Astilean, T. Iliescu, Raman and SERS Investigations of Pharmaceuticals; Springer Verlag, Germany, 2008.
- [5] S. Fornasaro, F. Alsamad, M. Baia, et al. Anal. Chem. 2020, 92, 4053–4064.

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## **Drug Delivery Nanosystems for Modern Targeted Therapy**

#### Josef JAMPILEK<sup>1,2</sup>

 Faculty of Natural Sciences, Comenius University, Ilkovicova 6, 84215 Bratislava, Slovakia
 Faculty of Science, Palacky University, Slechtitelu 27, 78371 Olomouc, Czech Republic josef.jampilek@gmail.com

Each active pharmaceutical ingredient (API) is formulated into a dosage form for administration for the purpose of treatment or diagnosis, which corresponds to the desired method of application/route of administration and whose main function is to enable or facilitate the production/preparation, storage and administration of drugs, and whose properties also favourably influence the behaviour of the API (drug) in organism. Dosage forms can be differentiated into multiple generations, with the use of next-generation drug delivery systems (with controlled release and targeted distribution) improving the efficacy of many existing APIs and enabling the introduction of new therapeutic approaches. The effort to miniaturize them from macrodimensions (>1 mm) to micro-, submicro- to nano-dimensions can be traced back to the 1990s, with great progress in recent years with the massive onset of nanotechnology. Various nanoemulsions of lipidoid formations or colloidal nanodispersions are very popular, i.e. nanoliposomes, solid lipid nanoparticles and other nanovesicles, dendrimers, polymer systems, tubules and quantum dots are used as drug carriers. Currently, drug delivery nanosystems made of non-toxic biodegradable biomaterials are preferred, however, in the case of nanoformulations for cancer therapy or diagnosis, inorganic nanocarriers made of metals/metal oxides, metalloids or carbon are also used, which often potentiate the effect of the API itself. Nanosystems for drug delivery enable targeted distribution to be easily achieved, whether it is a passive distribution, based on the size of the nanosystem or the EPR effect, or active, i.e. based on the modification of the surface of the nanoparticles, or in the case of a so-called magnetic nanoparticle, the application of an external magnetic field. The contribution is focused on a brief introduction to systems enabling the innovative administration of drugs already in clinical use, especially in the therapy of infectious and inflammatory diseases and cancer.

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## Plasmonic-based Nanoplatforms for Light-Activated Therapy, Bioimaging and Sensing

#### Simion ASTILEAN<sup>1,2</sup>

- <sup>1</sup> Department of Bimolecular Physics, Faculty of Physics, Babes-Bolyai University, 40084 Cluj-Napoca, Romania;
- <sup>2</sup> Nanobiophotonics and Laser Microspectroscopy Center, Interdisciplinary Research Institute in Bio-Nano-Sciences, Babes-Bolyai University, 40084 Cluj-Napoca, Romania simion.astilean@phys.ubbcluj.ro

Owning many advantages such as unique optical properties, easy surface modification and high biocompatibility, plasmonic nanoparticles have attracted enormous scientific interest in the biomedical field. In this presentation, we give an overview on our current approaches in fabrication and implementation of plasmonic-based nanoplatforms in a large variety of applications ranging from cell imaging and sensing to drug delivery and light-activated nanotherapeutics. For instance, several classes of biopolymer-coated plasmonic nanoparticles were implemented as versatile nanoprobes for spectroscopic investigation of cells by intracellular imaging via surface-enhanced Raman scattering (SERS), localized surface plasmon resonant scattering (LSPR-S) and steady-state and fluorescent lifetime imaging (FLIM). Scanning confocal Raman microscopy combined with dark-field and confocal fluorescence microscopy were used to record relevant intracellular information as nanoparticle localization, local chemical interaction, and intracellular pH mapping. In recent years, our research group has implemented several "proofs of concept" for light-activated nanotherapies against cancer by integration plasmon-induced photothermal therapy (PTT), plasmon-enhanced photodynamic therapy (PE-PDT) and delivery of chemotherapeutic drugs (doxorubicin, cisplatin) [1]. In the last years we focused on the development of new near-infrared (NIR) fluorescent nanoprobes able to perform as contrast agents for real-time image-guided surgery of ovarian cancer [2], as well fabrication of atomic gold nanoclusters and their implementation in the biomedical and sensor fields [3].

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#### References:

[1] S. Suarasan, A-M Craciun, E. Licarete, et al., ACS Appl. Mater. Interfaces 2019, 11, 7812–7822.

[2] R. Borlan, M. Focsan, M. Perde-Schrepler, et al., Biomater. Sci. 2021, 9, 6183.

[3] A.-M. Hada, A.-M. Craciun, M. Focsan, et al., Talanta 2021, 225, 121960.

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# Modified Electrodes with Nanostructured Carbon and/or Metallic Composites for Applications in Electroanalysis

#### Orlando FATIBELLO-FILHO

Department of Chemistry, Federal University of São Carlos, 13565-905 São Carlos, SP, Brazil bello@ufscar.br

This webinar will focus on modified electrodes with nanostructured carbon and/or metallic composites for applications in electroanalysis. The production, characterization and electrochemical properties of carbon and/or metallic materials will be discussed, following by a brief comparison with several carbon electrode materials. Nanocomposites present interesting properties, and these are improved with the incorporation of several nanomaterials in the forms of nanofilms, nanocoatings, nanofibers and, nanoparticles. Specially, carbon-based nanocomposites are extremely attractive materials for the development of electrochemical sensors and biosensors considering their features such as biocompatibility, fast electron transfer, and high specific surface area. Their importance in the preparation of (bio)sensors, and significant improvements in the analytical performance will be then addressed. Conclusions and perspectives of the use of those (bio)electrodes in electroanalytical will also be discussed.

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- [1] F.C. Vicentini, T.A. Silva, O. Fatibello-Filho, Curr. Opin. Electrochem. 2023, 43, 101415.
- [2] T.A. Silva, B. Lourencao, A.D. Silva, et al., Anal. Method. 2023, 15, 1077.
- [3] L.M.C. Ferreira, P.S. Silva, K.K.L. Augusto, et al., J. Pharmaceut. Biomed. 2022, 221, 115032.

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## Biosensing Approaches for Development of Innovative Analytical Systems for Agriculture, Food and Environmental Fields

#### Mihaela DONI and Ana-Maria GURBAN

National Institute for Research & Development in Chemistry and Petrochemistry, 060021 Bucharest, Romania

mihaela.doni@icechim.ro; ana-maria.gurban@icechim.ro

The use of composite nanomaterials in designing and development of (bio)sensitive tools undergoes a continuous expansion, leading to the development of new miniaturized sensing devices for fast and reliable infield determinations for various applications in environment, health and agri-food safety and security. Compared to traditional chromatographical methods, electrochemical (bio)sensing tools are portable, cheaper, easy to handle, reagentless and does not require trained personnel for on-site measurements.

Conducting nanomaterials have been used for decades to modify electrochemical sensors to enhance their electron transfer properties, increasing the active surface area, thereby improving analytical performance toward target analytes. Among the most used composite nanomaterials, the one based on carbon allotropes, metal nanoparticles and different polymer matrices (chitosan, sol-gel) have demonstrated high performances, with a reduced complexity in the functionalization of different templates of the electrochemical sensors.

The design and development of miniaturized electrochemical bioanalytical tools based on the advance in nanomaterial technology allow the achievement of unique features and diverse functionalities for various promising fields of applications: food quality control, environmental monitoring, point-of-care sensors for clinical diagnostic, flexible energy storage device, *etc*. Although nanomaterials are already found in many quotidian products, such as sports equipment, cosmetics, coatings, new nanomaterials with enhanced opto-electrochemical properties are still emerging, and their uses are frequently appearing in innovative applications such as catalysts, electronics, solar panels, batteries and biomedical applications including diagnostic devices and tumor therapies.

Nanocomposite materials based on carbon nanotubes, metallic nanoparticles and polymeric matrices (chitosan, hydrogels) were used for the development to simple and affordable miniaturized screen-printed (SPEs) based electrochemical (bio)sensors for determination of some relevant compounds such as mycotoxins, nitrite, heavy metals and biogenic amines in soils and food products.

Mycotoxins, the secondary products of the parasitic fungi, such as Aspergillus, Fusarium and Penicillium developed in plants are cytotoxic, inducing significant risks to the safety of nutrition, producing a breakdown

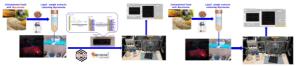


Fig. 1. SPR-ELEC detection of Aflatoxin M1.

of cell membranes and influencing the protein synthesis. An innovative combined surfaceplasmon resonance electrochemical platform integrated into an on-line flow

immunoassay configuration for sensitive and selective detection of aflatoxin M1 (AFM1) in milk has been developed (Fig. 1).

The immunosensitive layer consists in a copolymer film of 2, 6—dihyroxynaphtalene and 2, (4-aminophenyl) ethylamine entrapping the specific antibody to AFM1, electropolymerized onto the gold working electrode on a glass support. The properties of this immunosensitive film can be easily controlled through the electrodeposition parameters, while the immunorecognition process can be monitored simultaneously by the two detection techniques. The principle of AFM1 detection from liquid samples using the combined dual

detection platform is based on surface direct competition for the binding sites of the specific anti-AFM1 antibody immobilized in the polymeric film, between bioconjugate AFM1-HRP and target analyte AFM1. The immuno-recognition process is monitored indirectly, by electrochemical detection of the enzyme activity of horseradish peroxidase (HRP) used as marker in bioconjugate, and directly, by optic detection using surface plasmon resonance (SPR).

Nitrite, an indicator of the nitrification process in soils, was assessed by using a multiwalled carbon nanotubes (MWCNT)-chitosan based SPE sensor. The modified sensor facilitated the sensitive and rapid determination



Fig. 2. Electrochemical determination of nitrite in soil solution samples using MWCNT-CS based sensors.

from different types of soils used to grow plants, using portable devices. The detection of nitrite was achieved using MWCNT-CS-modified SPE sensors, in acetate buffer at pH 5, at an applied potential of 0.58 V vs. Ag/AgCl. The MWCNT-CS-based sensor displayed a specific sensitivity of 204.4 mA·M<sup>-1</sup>·cm<sup>-2</sup>, with a detection limit of 2.3  $\mu$ M (S/N = 3) in a linear range up to 1.7 mM. The miniaturized portable system using the MWCNT-CS-based sensors was used for the detection of nitrite in different samples of soil solutions extracted by using suction lysimeters (Fig. 2).

of nitrite in samples extracted with suction lysimeters

Biogenic amines, used as indicators of food spoilage and stress in plants, were determined using amperometric biosensors based on entrapment of the amine oxidases in sol-gel and chitosan-based polymeric matrices and immobilized on SPEs modified with a nanocomposite material based on the redox mediator Prussian blue (PB) and single-walled carbon nanotubes (SWCNT). Detection of

putrescine and histamine in meat products, cheese

Fig. 3. Assessment of biogenic amines using nanocomposites based electrochemical biosensors.

and beverage samples, as well as in soil solutions used to grow plants was achieved with good performances (Fig. 3).

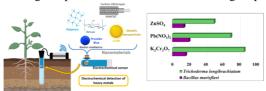


Fig. 4. Electrochemical detection of heavy metals using nanomaterial-based sensor and estimation of bioremediation capacity of metal-resistant microbial strains.

The amperometric detection putrescine was achieved using diamine oxidase entrapped in a sol-gel matrix on SWCNT-PB/SPEs, with a specific sensitivity of 153.7 mA·M<sup>-1</sup>·cm<sup>-2</sup>, a detection limit of 4.7 µM and a quantification limit of 15.5 µM, with a linear range extended from 0.02 and 1 mM, at an applied potential 0.05 V vs.

Ag/AgCl, PBS 0.1 M, pH 7.2. Determination of histamine was carried out using monoamine oxidase entrapment in chitosan polymeric matrix on SWCNT-PB/SPEs, with a specific sensitivity of 6.25 mA·M<sup>-1</sup>·cm<sup>-2</sup> and a detection limit of 57 μM.

Electrochemical sensors based on different nanomaterials such as PB, gold nanoparticles, MWCNT and chitosan were used to assess the chromium, lead and zinc in contaminated soils (Fig. 4).

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## Nanostructured Antibacterial Films by Ionized Jet Deposition: An Overview

#### Gabriela GRAZIANI

Polytechnic University of Milan, 20133 Milan, Italy gabriela.graziani@polimi.it

Infection is among the main complications connected to orthopaedic and dental implants and show important cross-relations with osteointegration. To address infection, functionalization of the biointerface by nanostructured metal-based coatings is a promising approach, as it permits to tackle bacteria without pushing towards the development of resistant bacterial strains. To this aim, metals can be used alone, or incorporated in calcium phosphates, to promote osseointegration. Together with composition, the morphological characteristics of the coatings are important, to avoid cracking and obtain a tuned release, both avoiding cytotoxicity.

Here, we propose the use of silver, copper and zinc-based nanostructured coatings, obtained by Ionized Jet Deposition. Films morphological (FEG-SEM, AFM) and compositional (EDS, XRD) characteristics are studied, and correlated to their antibacterial efficacy (inhibition of planktonic growth, of bacterial adhesion to the substrate and of biofilm formation, *E. coli*, *S. aureus*, *E. faecalis*, *P. aeruginosa*). The latter are studied by a specifically developed evaluation setup, based on the Calgary Biofilm Device.

Deposition of metal-doped calcium phosphates coatings (Ag-TCP) is also shown, demonstrating the feasibility to deposit complex materials while preserving their stoichiometry. Stability and antibacterial efficacy of the coatings is demonstrated and absence of cytotoxicity (reduction of cells viability or capability to differentiate) is studied on mesenchymal stem cells (MSCs).

Finally we show that the coatings can be deposited onto heat-sensitive substrates, including electrospun patches (Poly(L-lactic acid) - PLLA, Nylon - PA, medical grade polyester polyurethane - PU), without causing damage.

Our results show that silver films are composed by metallic silver, while oxides are obtained starting from copper and zinc targets. All films have a nanostructured surface morphology, where the size, shape and dimensions of the aggregates that compose them, as well as their thickness, strongly depend on the characteristics of the deposition target. All films are non-cytotoxic

Antibacterial efficacy of the films is strain- and metal- dependent, with silver being more efficient against Gram negative strains, and copper and zinc against Gram positive ones. In addition, the different metals impact differently on the different growth mechanisms of bacteria. The thickness and surface morphology of the films, both being dependent on deposition duration are also crucial in determining bacterial response to the coatings. After proper optimization, all films show high antibacterial efficacy, in terms of inhibition of planktonic growth, bacterial adhesion and biofilm formation.

Composite films preserve the composition of the target, although crystallinity is significantly reduced. Silver doping is also preserved, although its presence is reduced compared to the target. Even in the absence of thermal treatments the stability of the films is over 14 days in simulated medium. Silver-TCP films show high antibacterial efficacy and are non-cytotoxic.

Results show that the proposed films are promising for antibacterial functionalization of orthopaedic and dental implants.

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## **Functional Nanostructured Materials for Biomedical Applications**

#### Monica FLORESCU\* and Melinda DAVID

Transilvania University of Braşov, 500036, Braşov, Romania.

\*florescum@unitbv.ro

Nanomaterials have an increased versatility and multifunctionality and they can fulfil several roles, such as catalysts, amplifiers of electrical conduction or molecular recognition component, but also as nano-carriers for molecules. Thus, functional nanostructured materials can be obtained and used in the development of molecular detection and delivery platforms, playing a crucial role, topics that will be presented in this work. The use of biomolecules, like enzymes, in biosensors as analytical tools, offer big advantages for real-time detection due to their high specificity, selectivity, and quick response. They must be immobilized on different surfaces through processes that reduce the enzymatic activity. Nanozymes are nanomaterials with enzyme-like characteristics, and they can address the limitations of natural enzymes. In this talk, biomolecular analysis using natural enzyme-based biosensors versus nanozyme-modified sensors are evaluated and discussed. Carbon and metallic nanoparticles were employed as functional nanomaterials and evaluated for analytical

For drug delivery systems, an efficient approach for functional nanostructured materials was ascertained in different configurations [3,4]. Albumin proteins and liposomes were used as nanoparticles (NPs). The binding mechanism and affinity of the interaction between NPs with drug, and the effects of other biomolecules on the NPs-drug complex are evaluated and discussed for future development of efficient drug delivery systems.

#### References:

- [1] M. David, A. Şerban, T.A. Enache, et al., J. Electroanal. Chem. 2022, 911, 116240.
- [2] M. David, A. Serban, C. Radulescu, et al., Bioelectrochem. 2019, 129, 124.
- [3] N. Cazacu, C.G. Chilom, M. David, et al., Int. J. Mol. Sci. 2022, 23, 4215.

detection of drugs and antioxidant capacity of real samples [1,2].

[4] C.G. Chilom, M. David, M. Florescu, Spectrochim, Acta A. 2020, 230, 118074.

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#### INVITED ORAL PRESENTATION

# Detection, Identification and Structural Study of Biomolecules by Surface Enhanced Raman Spectroscopy

# A. AZZIZ<sup>1</sup>, M. MAJDINASAB<sup>1</sup>, C. ARIB<sup>1</sup>, Q. LIU<sup>1</sup>, D. STOIA<sup>2</sup>, M. FOCSAN<sup>2</sup>, M. EDELY<sup>1</sup>, Marc LAMY DE LA CHAPELLE<sup>1,2\*</sup>

<sup>1</sup> IMMM - UMR 6283 CNRS, Le Mans Université, Avenue Olivier Messiaen, 72085 Le Mans, Cedex 9, France
<sup>2</sup> Nanobiophotonics and Laser Microspectroscopy Center, Interdisciplinary Research Institute in Bio-Nano-Sciences, Babes-Bolyai University, Cluj-Napoca, Romania
\*marc.lamydelachapelle@univ-lemans.fr

The development of reliable, sensitive and specific biosensors is a very active research field. Among all the techniques, the Surface Enhance Raman Scattering (SERS) is one of most sensitive and has been widely used for ultrasensitive chemical analysis down to single molecule detection [1]. SERS is based on the exploitation of the optical properties of metallic nanoparticles and on the electromagnetic field enhancement localised at the vicinity of the nanostructures and created by the excitation of the Localized Surface Plasmon (LSP).

First, by controlling LSP, we are able to produce a highly sensitive sensor. We have determined the sensor characteristics such as its detection limit and its selectivity. We have determined that such sensor could be highly sensitive by reaching some detection limits lowest than the pico-molar. In this work, we have applied this sensor to the detection and the identification of specific proteins and we have been able to detect some specific disease biomarkers in body fluids (serum, saliva) paving the way to the potential disease diagnosis [2,3].

Second, the biosensor specificity is provided by multiple and simultaneous biomolecular recognition events based on weak interactions which give an apparent affinity. Aptamers, single DNA strands, are new bioreceptors intensively used now in biosensor. Through the self-hybridisation of one part of its sequence, the aptamer forms a loop structure exposing some bases that interact specifically with the analyte thanks to electrostatic interactions. It is of primary importance to understand such interaction to optimize the analyte capture and to improve the sensing performances. In addition, molecular interactions are the basis of many biological mechanisms. It is therefore important to have a better understanding of these phenomena and to be able to answer to specific questions as: how does the interaction take place?, is it dynamic or static?, is there any specific conformation for the interaction? To answer to such questions, we study the interaction between aptamer or DNA strand with its analyte or its complementary strand by the combination of SERS and multivariate statistical analysis. We observe the DNA structure and its evolution during the interaction under different experimental conditions (in air or in buffer) and we are able to probe the strand conformations and orientations relatively to the surface [4]. We also study the interactions between two DNA complementary strands (PolyA/PolyT) as well as strands containing mismatch in their sequences (one C base inserted at different positions in the sequence of polyA). We interpret the modification of the SERS spectra by some changes in the orientation and in the flexibility of the DNA strands during the hybridisation. Using Principal Component Analysis, we were able to determine some spectral markers of the hybridisation and of its disruption due to the single base mismatch. This study provides a new approach for the reliable quantification and structural analysis of biological molecules.

Acknowledgements: This work was supported by the European project DeDNAed (H2020-FETOPEN2018-2020, n° 964248) and by the project "Plasmon mediated biology: Exploitation of plasmonics to investigate and enhance biological processes and application to biomedical issues (acronym: BioPlasmonics)" funded by European Union – NextgenerationEU and Romanian Government, under National Recovery and Resilience Plan for Romania, contract no760037/23.05.2023, cod

PNRR-C9-I8-CF-199/28.11.2023, through the Romanian Ministry of Research, Innovation and Digitalization, within Component 9, Investment I8.

- [1] K. Kneipp, Y. Wang, H. Kneipp, et al., Phys. Rev. Lett. 1997, 78, 1667–1670.
- [2] M. Cottat, C. D'Andrea, R. Yasukuni, et al., J. Phys. Chem. C 2015, 119, 15532–15540.
- [3] R. Yasukuni, R. Gillibert, M.N. Triba, et al., Nanophotonics 2019, 8, 1477–1483.
- [4] W. Safar, A.S. Tatar, A. Leray, et al., Nanoscale 2021, 13, 12443–12453.

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### INVITED ORAL PRESENTATION

# Novel Therapeutic Approaches for the Management of Malignant Wounds

# Mariana Carmen CHIFIRIUC\*, Alexandra NICULESCU, Mihaela GEORGESCU, Ioana Cristina MARINAS

Faculty of Biology, University of Bucharest, 050095 Bucharest, Romania \*carmen.chifiriuc@bio.unibuc.ro

Malignant fungating wounds are a very severe and challenging condition associated with advanced cancer stages, impoverishing the patient with pain, malodor, exudation, pruritus, edema, and bleeding. As the classical therapeutic approaches are often failing to handle the symptoms, alternative strategies are urgently needed. The aim of this presentation is to provide an update on the contribution of nanotechnology and materials science to the development of innovative treatment approaches.

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### INVITED ORAL PRESENTATION

# Redox Gradients in Materials and Unwired Bipolar Electrodes in Neural Systems

### Nieves CASAÑ-PASTOR

Institut of Materials Science of Barcelona, CSIC, Campus UAB, 08193 Bellaterra, Barcelona, Spain nieves@icmab.es

Electrical activity underpins all life, but is most familiar in the nervous system, where long range electrical signalling is essential for function. The use of external fields can compensate for at least some functional deficits, if they occur. However, its potential to also promote repair at the cellular level has only been demonstrated *in vitro*. Although there is consistent evidence that external electric fields promote cell growth, not much attention is given to the electrode materials. Furthermore, electrodes are usually connected to the power source. Recently a new possibility has emerged. An external system may polarize a conducting material immersed in the bio-electrolytes, creating a bipolar unwired electrode with induced anode and cathode in opposite poles of the material.

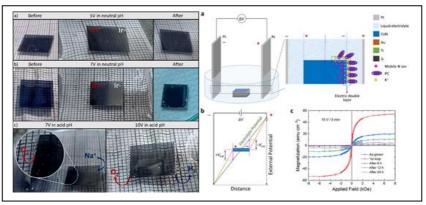


Fig. 1. Example of bipolar electrodes: Change in colour in IrOx and Ferromagnetism induced in CoN.

The use of a wireless method to create electrical interactions with a biological system represents a paradigm shift and may allow new applications *in vivo* where physical wiring is not possible. Several key aspects are observed: The global impedance changes in the cellular media when conducting materials are immersed even if no percolation does exist; the material itself, when mixed conducting systems are chosen, offers a significant redox and ionic gradient across, that expands stimulation in time even after the external field is off; changes in resistivity occur at the material that create complex dipoles and oscillating behaviours. Therefore, neurons are exposed to a variety of voltage gradient profiles, depending on the material and the electric field protocol. As a consequence, different neural behaviours are observed. In some cases, the speed of growth is enhanced, while in others, neurite growth turns towards one of the poles. This work will show a summary of the local resolution studies that evidence the redox and ionic gradients. Finally, additional properties with influence on the biological system are considered, like the *in-situ* generation of volatile or permanent ferromagnetism on the material implanted, with possible future applications. This strategy emphasizes how nerve growth can be encouraged at injury sites wirelessly to induce repair, and how we may benefit from the induced fields in polarized conducting materials to achieve localized therapies.

- [1] A. Rajnicek, N. Casañ-Pastor, Biomaterials Science, 2023, in press.
- [2] Z. Ma, L. Fuentes-Rodriguez, N. Casañ-Pastor et al., Nature Comm. 2023, 14, 6486.
- [3] L. Fuentes-Rodríguez, N. Casañ-Pastor, Mater. Chem. Frontiers 2022, 6, 2284.
- [4] L. Fuentes-Rodríguez, N. Casañ-Pastor, J. Electrochem. Soc. 2022, 169, 016508.
- [5] A.M. Rajnicek, C.Suñol, N. Casan-Pastor, Engineering Biomaterials for Neural Applications, Springer Nature, Chapter 5. 2021.
- [6] L. Fuentes-Rodriguez, N. Casañ-Pastor, J. Phys. Chem. C 2021, 125, 16629.
- [7] N. Casañ-Pastor, *Molecules* **2021**, *26*, 4236.

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# Abstracts of Poster Presentations

# PCL Electrospun Fibers as a New Biocompatible Platform for Ion Detection

# Anca ALDEA<sup>1,\*</sup>, Melania ONEA<sup>1,2</sup>, Daniela OPREA<sup>1,2</sup>, Daniel CRISAN<sup>1</sup>, Caroline SANZ<sup>1</sup>

- <sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania
- <sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

Sweat contains a large range of electrolytes that have important roles in the body [1,2] and provides multiple health information. In sweat, the most abundant electrolytes are sodium and chloride which can be used as diagnostic tool in, for example, cystic fibrosis [3], but potassium, magnesium, and calcium are also found, albeit in smaller amounts. Beside these, other biomarkers are small molecules (cortisol, urea, lactate, glucose, uric acid etc.) and peptides or even proteins (neuropeptides and cytokines).

Ionophores are small molecules specific and selective for certain ions. By incorporating specific ionophores in the construction of the sensors can be obtained selective sensors for each type of ion found in different samples. In order to perform sweat analysis one important criteria is the flexibility of the substrate. In this work, polycaprolactone electrospun fibers were obtained, metallized and used as a platform for a new wearable sensor for sweat analysis.

The targeted electrolytes were  $Na^{2+}$ ,  $K^+$ , and  $Cl^-$ , and their detection and measurement were accomplished using various ionophores embedded in lipid membranes. Different procedures and synthesis methods were involved in the incorporation of the ionophores in the membranes. As precursors for the lipidic membrane DPPC and OSPC were used in order to synthesis liposomes.

SEM with energy-dispersive X-ray spectroscopy, Fluorescence Microscopy (Figure 1), Raman Spectroscopy, Fourier-Transform Infra-Red Spectroscopy, cyclic voltammetry, and electrochemical impedance spectroscopy were used to characterize the interface. The obtained potentiometric electrochemical sensors served for ions determination and quantification in different media. Sensitivity and detection limit of the sensors were determined.

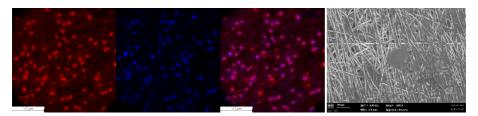


Fig. 1. Fluorescence and scanning electron microscopy (SEM) images of potassium ion sensor on which L929 fibroblast cells were seeded and grown.

Acknowledgements: Financial support from the Executive Agency for Higher Education, Research, Development and Innovation Funding (UEFISCDI), Romania, Project code: PN-III-P1-1.1-PD-2021-0319.

- [1] A. Aldea, E. Matei, R.J.B. Leote, et al., Electrochim. Acta 2020, 363, 137239.
- [2] A. Aldea, R.J.B. Leote, E. Matei, et al., Microchem. J. 2021, 165, 106108.
- [3] S.C. Bell, M.A. Mall, H. Gutierrez, et al., Lancet Respir. Med. 2020, 8, 65–124.

<sup>\*</sup>anca.aldea@infim.ro

# **Graphene Electronic Devices for Sensing Applications**

# Mariana Mihaela APOSTOL<sup>1,2,\*</sup>, Elena MATEI<sup>1</sup>, Victor DICULESCU<sup>1</sup>, Ionuț ENCULESCU<sup>1</sup>, Issam BOUKHOUBZA<sup>1</sup>

<sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

Graphene, a single layer of carbon atoms arranged in a hexagonal lattice holds immense potential in various fields of science, medicine and technology [1,2] due to its unique physico-chemical properties. Graphene's high surface area, electrical conductivity, and biocompatibility make it an excellent material for biosensors. Functionalization of the graphene surface with bio-recognition elements among which nucleic acids, antibodies or aptamers is essential for specific detection of biomolecules such as proteins, DNA, RNA, or small molecules of biological relevance. Changes in the electrical conductivity of graphene results from the binding of target molecules, ad this parameter can be used as analytical signal for their sensitive detection [3]. The objective of this research was the synthesis of graphene layers on copper substrate by Chemical Vapor Deposition (CVD), the transfer of graphene from the copper substrate onto gold electrode systems, followed by physical and chemical characterization and application to the development of electrochemical immunosensors. Raman Spectroscopy and Scanning Electron Microscopy (SEM) were used in tandem for graphene's characterization. In order to demonstrate the possibility of using the graphene layer in electronic devices for biosensors, experiments were carried for its functionalization with antibodies toward prostate specific antigen (PSA). PSA detection was performed by electrochemical impedance spectroscopy.

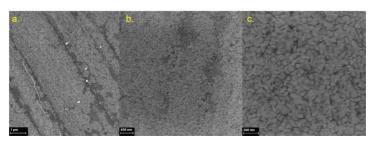


Fig. 1. SEM images of multilayer G on Au/glass substrate.

**Acknowledgements:** This work was supported by the Core Program of the National Institute of Materials Physics, granted by the Romanian Ministry of Research, Innovation and Digitalization under the Project PC1-PN23080101. **References:** 

- [1] B. Fadeel, C. Bussy, S. Merino, et al., ACS Nano 2018, 12, 10582–10620.
- [2] A.C. Ferrari, F. Bonaccorso, V. Fal'ko, et al., Nanoscale, 2015, 7, 4598-4810.
- [3] C. I. L. Justino, A.R. Gomes, A.C. Freitas, et al., TrAC, Trends Anal. Chem. 2017, 91, 53–66.

<sup>&</sup>lt;sup>2</sup> Faculty of Chemical Engineering and Biotechnologies, National University of Science and Technology POLITEHNICA Bucharest, 011061 Bucharest, Romania

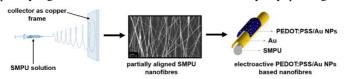
<sup>\*</sup>mariana.apostol@infim.ro

# Shape Memory Polymer Nanofibres Functionalized with PEDOT:PSS and Au Nanoparticles for Soft Robotics Applications

# Mihaela BEREGOI<sup>1,\*</sup>, Denisa CĂLIN<sup>2</sup>, Adrian ENACHE<sup>1</sup>, Ana Maria IGNAT<sup>1,3</sup>, Ionuț ENCULESCU<sup>1</sup>

- <sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania
- <sup>2</sup> Faculty of Medical Engineering, National University of Science and Technology POLITEHNICA Bucharest, 011061 Bucharest, Romania
- <sup>3</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

Bioinspired devices from soft robotics field, especially wearable sensors and actuators, have gained increasing attention in academic research and industrial development with the aim of improving the community way of life. Soft actuators are devices developed to perform a mechanical movement in response to an applied external stimulus, usually voltage, heat, light or magnetic field [1]. Materials used for designing soft actuators should meet various requirements like high flexibility, fast response time, low power consumption, low manufacturing costs and straightforward procedures, light weight, long life time, *etc.* A lot of materials were developed to fulfil the mentioned requests such as electroactive polymers, hydrogels, dielectric elastomers, shape memory materials, etc. [2]. However, electroactive polymers, especially conducting polymers in the form of fibre morphology are preferred due to the high active area, high flexibility, fast response time under low applied voltages, revealing impressive actuation properties and even sensing capabilities during movement [3,4]. In this context, a novel material configuration based on shape memory polymer electrospun nanofibers (namely polyurethane with a transition temperature of 65°C, SMPU) and poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS) functionalized with Au nanoparticles (Au NPs) which can perform mechanical motion by applying an external stimulus is proposed. Thus, free standing partially aligned SMPU nets were covered with a thin Au layer by sputtering and then a PEDOT:PSS film



Scheme 1. Preparation of electroactive SMPU fibres.

with dispersed Au NPs was deposited on top of the fibres through electrochemical synthesis (according to *Scheme 1*). The

prepared material was morphologically, structurally, mechanically analyzed and from biocompatibility and actuation point of view. The shape memory behaviour and addition of Au NPs should improve the actuation performances by increasing the conductivity of the material and therefore the voltage/temperature distribution along the fibres.

 $\label{lem:constraint} \textbf{Acknowledgements:} \ This work \ was \ supported \ by \ the \ Romanian \ Ministry \ of \ Research, \ Innovation \ and \ Digitalization \ through \ the \ Projects \ PC1-PN23080101.$ 

- [1] R.J.B. Leote, M. Beregoi, I. Enculescu, V.C. Diculescu, Curr. Opin. Electrochem. 2022, 34, 101024.
- [2] I. Apsite, S. Salehi, L. Ionov, Chem. Rev. 2022, 122, 1349–1415.
- [3] M. Beregoi, A. Evanghelidis, V. Diculescu, H. Iovu, I. Enculescu, ACS Appl. Mater. Interfaces 2017, 9, 38068–38075.
- [4] M. Beregoi, S. Beaumont, A. Evanghelidis, T.F. Otero, I. Enculescu, Sci. Rep. 2022, 12, 15019.

<sup>\*</sup>mihaela.oancea@infim.ro

# Paper-based Electrochemical Device Integrated with Conductive Submicron Polymeric Fibers and 3D Printed Channels

# Daciana BOTTA $^{1,2*}$ , Mihaela BEREGOI¹, Alexandru EVANGHELIDIS¹, Elena MATEI¹, Ionut ENCULESCU¹, Victor C. DICULESCU¹

<sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

Flexible porous materials such as paper or textiles gained an increased interest in the last decade due to their property of passively driving the fluids under the capillary force, as well as the possibly of loading and storing reagents in their matrix. The common approach in the fabrication technology of a paper-based electrochemical cell is to integrate screen-printed or sputtered electrodes with a wax patterned porous substrate. While these represent facile and affordable methods, they present some critical disadvantages, the most important being the low reproducibility of the resulting electrodes [1]. Metallized electrospun polymeric fiber meshes were shown to be great alternatives for flexible electrodes in (bio)sensing applications, due to their high surface-tovolume ratio given by the submicronic features of the fibers [2]. Moreover, the possibility of creating conductive surfaces on paper by thermally transferring the metallized fibers was previously demonstrated [3]. In this work, the possibility of integrating metallized fiber meshes with chromatographic paper for the development of an electrochemical cell was demonstrated. The chromatographic paper was 3D patterned with wax-alike polymers, in order to provide a hydrophobic barrier for fluid confinement. The conductivity of the fibers was ensured by magnetron sputtering deposition of gold, silver, platinum, or palladium. The morphology of the fibers and the paper, as well as their assembly after the thermal treatment, was studied by scanning electron microscopy revealing a high degree of structural integrity of both components. In order to achieve high stability, the electrochemical cell was developed in a three-electrode configuration. This was achieved by fabricating 3D printed masks, which provided a rapid and unexpensive means of selectively patterning the fiber meshes with metal layers, enabling the possibility of creating multiple electrodes from a single fiber mesh. Moreover, in order to provide mechanical resistance of the paper-based device and good ohmic contact with the electrodes, a 3D printed holder with copper or platinum contacting sheets was developed. The resulting electrochemical cell was characterized by cyclic voltammetry and electrochemical impedance spectroscopy in the absence and in the presence of redox probes such as K<sub>4</sub>[Fe(CN)<sub>6</sub>] and methylene blue. As proof of concept, the electrochemical paper-based device was tested for the amperometric detection and quantification of enzymatic reaction by-products such as H<sub>2</sub>O<sub>2</sub> and NADH, as well as analytes such as glucose in the presence of glucose oxidase.

Acknowledgements: Financial support from the Executive Agency for Higher Education and Research Funding (UEFISCDI) through project PN-III-P4-PCE-2021-1006.

- [1] D. Botta, I. Enculescu, C. Balan, V.C. Diculescu, Curr. Opin. Electrochem. 2023, 42, 101418.
- [2] R.J.B. Leote, D.N. Crisan, E. Matei, I. Enculescu, V.C. Diculescu, ACS Appl. Polym. Mater. 2024, 6, 2274–2283.
- [3] C. Busuioc, A. Evanghelidis, A. Galatanu, I. Enculescu, Sci. Rep. 2016, 6, 34584.

<sup>&</sup>lt;sup>2</sup>REOROM Laboratory, National University of Science and Technology POLITEHNICA Bucharest, 060042 Bucharest, Romania

<sup>\*</sup>daciana.botta@infim.ro

The Effect of Fullerene Layer on the Aggregates Formation in Amyloid beta Langmuir-Blodgett Films

# Carmen BREAZU<sup>1,\*</sup>, Oana RAȘOGA<sup>1</sup>, Marcela SOCOL<sup>1</sup>, Paul GANEA<sup>1</sup>, Teddy TTTE<sup>1</sup>, Elena MATEI<sup>1</sup>, Florin STĂNCULESCU<sup>2</sup>, Anca STĂNCULESCU<sup>1</sup>

The investigation of the effect of carbon nanomaterials and lipids on the aggregation particularities of the amyloid beta/ $\Delta\beta(1\text{-}42)$  layers is important for understanding the generation mechanism of neuronal disorder and how it can be inhibited. Additionally, amyloids are nanomaterials with a wide area of potential applications from nanotechnology to biotechnology. This paper presents a study about the preparation of  $\Delta\beta(1\text{-}42)$  layer by two different methods, Langmuir-Blodgett (L-B) and drop cast (DC), on Si and Si covered by a layer of Buckminster fullerene,  $C_{60}$ , and on the effect of fullerene layer or/and cholesterol (Ch) on the generation of  $\Delta\beta(1\text{-}42)$  secondary structure forms, relevant for specific applications. Microscopic (SEM-EDX, AFM, optical) and vibrational spectroscopy (FTIR, Raman) methods were used for the secondary structures analysis in correlation with layers' morphology and surface topography. This study showed that the presence of Ch inhibited the formation of fibrils in  $\Delta\beta(1\text{-}42)$  film deposited by L-B on Si covered by  $C_{60}$ . The structures developed during aggregation were correlated with the topography and roughness of the films. The presence of Ch determined a decrease in roughness for L-B film and increase in roughness for DC film deposited on Si covered by  $C_{60}$  layer.

<sup>&</sup>lt;sup>1</sup> National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

<sup>\*</sup>carmen.breazu@infim.ro

# Soft Actuators Based on Polydimethylsiloxane and Electrospun Fiber Networks

# Mihaela-Cristina BUNEA\*, Mihaela BEREGOI, Alexandru EVANGHELIDIS, Andrei GALATANU, Ionut ENCULESCU

National Institute of Materials Physics, 077125 Magurele, Romania.

Over the past two decades, development of new soft actuators based on dielectric elastomers for biomimetic implants are widely studied thanks to their adaptability and high flexibility [1]. Dielectric elastomers which belong to the electronic electroactive polymers class, present an important interest for various applications due to their lightweight, high energy density, fast actuation speed and large deformation through the conversion of the electrical energy into mechanical work [1,2]. This type of polymers are promising candidates for muscle-like actuators. Polydimethylsiloxane is one of the most used polymers from the dielectric elastomer category with various properties such as good elasticity, gas permeability, good biocompatibility and form conformal contact with surfaces [3,4]. Withal, electrospun fibers are an excellent reinforcement material, useful for manufacturing soft actuators due to their features like good flexibility, high specific area, good mechanical stability and easy to be obtained [1,4]. The aim of this study is to develop a new architecture of artificial muscles based on a web of metal covered nylon 6/6 micrometric fibers attached to a thin polydimethylsiloxane (PDMS) as possible candidates for biomimetic applications. The prepared materials were analyzed from morphological, electrical and mechanical stability point of view. Also, some of fabricated actuator skills were highlighted.

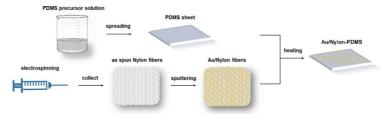


Fig. 1. Fabrication steps of PDMS artificial muscles.

- [1] M.C. Bunea, M. Beregoi, A. Evanghelidis, et al., Sci. Rep. 2022, 12, 13084.
- [2] J. Wang, D. Gao, P.S. Lee, Adv. Mater. 2021, 33, 2003088.
- [3] A.M. Baracu, M.A. Avram, C. Breazu, et al., Nanomaterials, 2021, 706, 24.
- [4] M. Aouraghe, Z. Mengjie, Adv. Fiber Mater. 2021, 3, 38-46.

<sup>\*</sup>mihaela.bunea@infim.ro

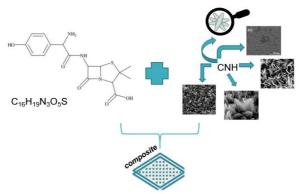
# Nanohybrid Composites of the type TiO<sub>2</sub>/Single-Walled Carbon Nanohorns for the Amoxicillin Photodegradation

# Radu CERCEL<sup>1,2\*</sup>, Andreea ANDRONE<sup>1</sup>, Cristina-Ștefania FLORICA<sup>1</sup>, Adam LORINCZI<sup>1</sup>, Constantin SERBSCHF<sup>3</sup>, Mihaela BAIBARAC<sup>1</sup>

<sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

\*radu.cercel@infim.ro

This study explores the potential applications of nanohybrid composites incorporating titanium dioxide (TiO<sub>2</sub>) with an anatase crystalline phase and single-walled carbon nanohoms (SWCNHs) as catalysts for the photodegradation of amoxicillin (AMOX) [1]. The TiO<sub>2</sub>/SWCNH composites were synthesized through the solid-state interaction of these chemical compounds. Altering the SWCNH concentration in the composite mass, by ranging from 1 wt.% to 5 wt.% and 10 wt.%, significant changes are reported. Specifically, variations were observed in the relative intensity ratio of Raman lines at 145 and 1595 cm<sup>-1</sup>, corresponding to the Eg(1) vibrational mode of TiO<sub>2</sub> and the graphitic structure of SWCNHs. Additionally, a gradual increase in the IR band absorbance at 1735 cm<sup>-1</sup> indicated the formation of new carboxylic groups on the SWCNHs' surface. The most effective photocatalytic properties were demonstrated for the TiO<sub>2</sub>/SWCNH composite with a 5 wt.% SWCNH concentration, achieving approximately 92.4% removal of AMOX after 90 minutes of UV irradiation. This superior performance is attributed to the presence of SWCNHs, acting as capture agents for the photogenerated electrons of TiO<sub>2</sub>, thereby impeding electron-hole recombination. The TiO<sub>2</sub>/SWCNH composite exhibited greater efficiency in AMOX photodegradation compared to TiO2 alone. The stability of the TiO2/SWCNH composite with a 5 wt.% SWCNH concentration was confirmed through six consecutive photodegradation cycles of a 98.5 µM AMOX solution. The efficiency slightly decreased from 92.4% to 78%, indicating the composite's robustness and suitability for repeated use.



Composites based on TiO2 and SWCNH for the amoxicillin degradation.

### Reference:

[1] R. Cercel, A. Androne, C.S. Florica, et al., Molecules, 2023, 28, 6958.

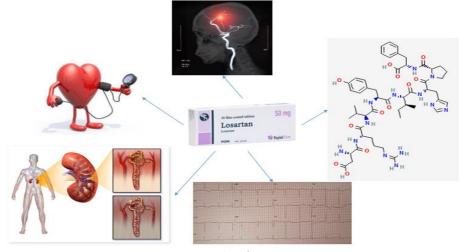
<sup>&</sup>lt;sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania<sup>3</sup>S.C. Bioelectronic S.R.L., 100028 Ploiesti, Romania

# Spectroscopic Studies Concerning Degradation of Losartan Potassium

# Mădălina CHIVU $^{1,2*}$ , Mirela PARASCHIV $^{1,2}$ , Ion SMARANDA $^1$ , Irina ZGURĂ $^1$ , Paul GANEA $^1$ , Bogdan CHIRICUȚĂ $^3$ , Mihaela BAIBARAC $^1$

<sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

Losartan potassium (LP) serves as the active ingredient within the pharmaceutical formulation known as Lorista (LO), prescribed for the management of hypertension and renal complications in individuals with diabetes and heart failure [1,2]. This contribution presents insights into the degradation patterns of LP under varying conditions, including exposure to UV light, the composition of phosphate buffer solutions (PBS) and an alkaline medium [3]. These issues are elucidated through a combination of analytical techniques including FTIR spectroscopy, photoluminescence analysis, and dielectric spectroscopy [3]. The degradation of solid-state LO is discernible by the intensity attenuation of the PL band at 380 nm. The phenomenon is attributed to the interaction of LP with water vapor in the storage medium of the drug.



Losartan's applications

- [1] A.C. Amenos, M.G. Diezhandino, F.D. Moreno, Nefrologia 2008, 28, 39-48.
- [2] L.M. Ruilope, L.C.Aldigler, C. Ponticelli, et al., J. Hypertens. 2000, 18, 89–95.
- [3] M. Paraschiv, I. Smarnada, I. Zgura, et al., Pharmaceutics 2022, 14, 2419.

<sup>&</sup>lt;sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

<sup>&</sup>lt;sup>3</sup>S.C. Apel Laser S.R.L., 077135 Mogosoaia, Romania

<sup>\*</sup>madalina.chivu@infim.ro

# BT-based Piezoceramics Substituted with Therapeutic Cations

Marius Cristian CIOANGHER<sup>1,\*</sup>, Liviu NEDELCU<sup>1</sup>, George E. STAN<sup>1</sup>, Luminita AMARANDE<sup>1</sup>, Corneliu Florin MICLEA<sup>1</sup>, Adrian-Claudiu POPA<sup>1</sup>, Lucia Nicoleta LEONAT<sup>1</sup>, Cristina BESLEAGA<sup>1</sup>, Cezar Dragos Geambasu<sup>1</sup>, Vasilica TOMA<sup>1</sup>, Irina Sorina GHITA<sup>1</sup>, Robert Catalin CIOCOIU<sup>2</sup>, Constantin MARIN<sup>3</sup>

Inducing faster healing of bone tissue affected by illness or trauma necessitates a multidisciplinary approach. The exploration of cationic substitutions in barium titanate (BT)-type ceramics aimed to achieve a synergistic chemical [1,2] and piezoelectric [3,4] stimulation of osteogenesis. In this regard, doping with Sr and Ga could enhance both the piezoelectric and osteogenic responses, while also potentially exhibiting angiogenic, antimicrobial, or anticarcinogenic properties. The research focused on studying eight compositions of barium titanate-type materials doped with Sr or Ga, with the stoichiometric formulas Ba<sub>1-x</sub>Sr<sub>x</sub>TiO<sub>3</sub> or Ba(<sub>1-3x2</sub>)Ga<sub>x</sub>TiO<sub>3</sub> respectively, where x = 2, 4, 6, and 8. Solid-state synthesis was employed to obtain the ceramics. Mixed raw materials were calcined at 1100 °C, followed by milling and sintering at 1400 °C for 20 minutes and then at 1350 °C for 3 hours. The two-step sintering process enabled obtaining BT ceramics with controlled grain growth and a tetragonal single phase, as evidenced by XRD characterization. SEM investigations revealed grain dimensions of approximately 20 µm for all materials doped with Ga, as well as for materials doped with 2 mol% and 4 mol% Sr. However, materials doped with 6 mol% and 8 mol% Sr exhibited reduced grain dimensions of around 5 µm. The ferroelectric measurements showed that for Ga-doped materials, losses due to conduction at high electric fields increase with the doping level, which is associated with a decrease in density. The highest value of remnant polarization for Sr-doped BTs was measured at 4 mol% Sr, with a value of 15 µC/cm² being obtained. Planar coupling factor kp and piezoelectric constants d<sub>33</sub> and d<sub>31</sub> tend to decrease with increasing Ga content. The best electromechanical and piezoelectric responses were obtained for the 4 mol% Ga BT. For Sr-doped BT ceramics, the coupling factor and piezoelectric constants decrease with increasing doping level, with the best properties observed for doping with 4 mol% Sr. An increase in compression resistance was observed in the BT doped with Ga 4 mol% (with ~26%), Sr 4 mol% (with ~70%) and Sr 6 mol% (with ~19%), compared to pure BT. The concentration of Sr and Ga ions released in cellular media was determined by ICP-MS, revealing that they are released in small quantities (<1 mg/L). MTS assays indicated good cell proliferation for all doped BT-type materials. LDH tests showed no detrimental increase in cellular death compared to control, irrespective of type of BT ceramic. Cells with normal morphology and nuclei dimensions were observed for all BTs, with a typical tendency to extend filopodia and lamellipodia.

Acknowledgements: This work was supported by Core Program, component project PN23080101, funded by Romanian Ministry of Research, Innovation and Digitization.

- [1] V.M. Schatkoski, L.T. do Amaral Montanheiro, B.R. Canuto de Menezes, et al., Ceram. Int. 2021, 47, 2999–3012.
- [2] T. Tite, A.C. Popa, L.M. Balescu, et al., Materials, 2018, 11, 2081.
- [3] A.K. Ulstrup, Acta Orthop. Belg. 2008, 74, 291-302.
- [4] Y. Uto, S. Kuroshima, T. Nakano, et al., PLoS One, 2017, 12, e0189893.

<sup>&</sup>lt;sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup> Department of Metallic Materials Science, National University of Science and Technology POLITEHNICA Bucharest, 060042 Bucharest, Romania

<sup>&</sup>lt;sup>3</sup> "Emil Racoviță" Institute of Speleology of the Romanian Academy, 050711 Bucharest, Romania

<sup>\*</sup>cmarius@infim.ro

# Yttrium Barium Copper Nano Oxide Synthesis for Biomedical Utilization

# Rania DAHA<sup>1,\*</sup>, Manel BOULOUDENINE<sup>2,3</sup>, Katia DJENADI<sup>4</sup>, Stefano BELLUCCI<sup>5</sup>

- <sup>1</sup> École Nationale Supérieure des Mines et de la Métallurgie (ENSMM)-Amar Laskri, L3M, Chainz, 23000 Annaba, Algeria
- <sup>2</sup>Mohamed-Cherif Messaadia University, 41000 Souk Ahras, Algeria
- <sup>3</sup>LPR, Laboratory, University Badji Mokhtar, 23000 Annaba, Algeria
- <sup>4</sup>Laboratoire de Biochimie Appliquée, Département des Sciences Alimentaires, Faculté des Sciences de la Nature et de la Vie, Université de Bejaia, 06000 Bejaia, Algeria
- <sup>5</sup>INFN-Laboratori Nazionali di Frascati, 00044 Frascati, Italy

This research focuses on the synthesis of YBa<sub>2</sub>Cu<sub>3</sub>O<sub>7</sub> (YBCO) via the Sol-Gel method and investigates the antibacterial properties of YBCO nanoparticles (NPs). Our study delves into the experimental nuances of NP synthesis, aiming to unveil the antibacterial potential of YBCO NPs, a high-temperature superconductor, against four distinct bacterial strains. Varied concentrations of YBCO NPs (0.01 mg/ml, 0.025 mg/ml, 0.05 mg/ml, and 0.1 mg/ml) were employed in testing. The synthesized NPs underwent thorough characterization utilizing advanced techniques, including X-ray diffraction (XRD), scanning electron microscopy (SEM), differential scanning calorimetry (DSC), and thermogravimetric (TG) analysis.

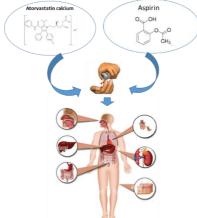
Remarkably, Gram-positive strains, specifically *Staphylococcus epidermidis* and *Methicillin-resistant Staphylococcus aureus* (MRSA), demonstrated heightened susceptibility to YBCO NPs, while Gramnegative strains exhibited a subdued response. Intriguingly, even at elevated concentrations, these bacterial strains displayed persistent resistance. Our findings shed light on the promising potential of YBCO NPs as an effective antibacterial agent against specific pathogens. This research contributes valuable insights to the field, emphasizing the multifunctional applications of YBCO NPs.

<sup>\*</sup>rania.daha@ensmm-annaba.dz

# Photodegradation of Aspirin and Atorvastatin Calcium Revealed by Photoluminescence Studies

# Monica DĂESCU<sup>1,\*</sup>, Miruna IOȚA<sup>1</sup>, Constantin SERBSCHI<sup>3</sup>, Alina C. ION<sup>2</sup>, Mihaela BAIBARAC<sup>1</sup>, Mădălina OPRICĂ<sup>1</sup>, Szilard FEJER<sup>4</sup>

Recently, photodegradation processes have been of great interest in the field of pharmaceuticals. Many drugs are sensitive to UV light and can react with excipients or atmospheric oxygen to form toxic compounds that can interfere with therapeutic activity. Light can affect the active ingredient of the drug as well as the packaging in which the final product is contained [1]. Atorvastatin calcium [2, 3] and Aspirin [4, 5] are drugs used to treat cardiovascular disease, such as a heart attack or stroke. The novelty of this work consists in monitoring the photodegradation of atorvastatin calcium and aspirin using photoluminescence (PL). In this work, new optical evidences regarding the photodegradation process of aspirin and atorvastatin calcium, in the presence of alkaline medium as well as phosphate buffer, will be reported by PL, UV–Vis spectroscopy, Raman scattering and FTIR spectroscopy.



The role of aspirin and atorvastatin calcium in the body.

- [1] D. Pluskota-Karwatka, M. Hoffmann, Curr. Org. Chem. 2018, 22, 1926–1939.
- [2] M. Niazi, N. Galehdar, M. Jamshidi, et al., Curr. Clin. Pharmacol. 2020, 15, 30–37.
- [3] M. Oprica, M. Iota, M. Daescu, et al., Sci. Rep. 2021, 11, 115338.
- [4] S.V. Ittaman,; J.J. VanWormer, S.H. Rezkalla, Clin. Med. Res. 2014, 12, 147–154.
- [5] M. Daescu, M. Iota, C. Serbschi, et al., Int. J. Mol. Sci. 2021, 22, 4046.

<sup>&</sup>lt;sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup> Faculty of Chemical Engineering and Biotechnologies, National University of Science and Technology POLITEHNICA Bucharest, 011061 Bucharest, Romania

<sup>&</sup>lt;sup>3</sup>S.C. Bioelectronic S.R.L., 100028 Ploiesti, Romania

<sup>&</sup>lt;sup>4</sup>Pro-Vitam Ltd., 520032 Sfantu Gheorghe, Romania

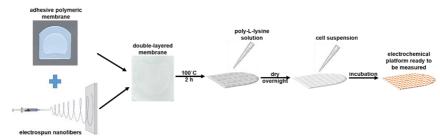
<sup>\*</sup>monica.daescu@infim.ro

# Electrospun Fibrillary Scaffold for Electrochemical Cell Biomarkers Detection

# Adrian ENACHE $^{1,*}$ , Mihaela BEREGOI $^1$ , Daniela OPREA $^{1,2}$ , Mihaela Cristina BUNEA, Monica ENCULESCU $^1$

- <sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania
- <sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

The most amazing biological structure is the living cell, a dynamic machine that integrates a wide variety of biochemical structures, continuously adapting and responding to the local environment. The cellular systems produce and transform signaling biomarker molecules to inter-communicate, and their integration in biosensing devices became an important tool to understand the underlying mechanisms of different diseases, as well as to perfect timely disease diagnosis and personalized therapeutic approaches. Electrochemical methods, especially voltammetry and the related techniques have appropriate features to be used as monitoring methods for biosensor systems. This kind of sensors are well described in the literature, have many embodiments that make them specific for certain parameters detection and quantitative determination. The electrochemical biosensors for continues and real-time monitoring the cell cultures represent an upright experimental model that have many embodiments. One should be considered, the electrochemical sensing of cell biomarkers requires the cultivation of the cells on/near the (bio)sensor surface in a manner to preserve an appropriate electroactive available surface, and to avoid the surface passivation and sensor damage. This can be achieved by employing biocompatible nanofiber meshes that allow the cells to have a normal behavior and do not alter the electrochemical detection. For a better mechanical stability and ease of handling, nylon 6/6 nanofibers were collected on commercial polymeric membranes, at an optimal fiber density, obtaining a double-layered platform, Scheme 1.



Scheme 1. Preparation steps of the electrospun fibrillary scaffolds for cell culture support.

To demonstrate the functionality of the fabricated scaffold, the screening of cellular stress has been achieved integrating melanoma B16-F10 cells and the (bio)sensor components on the transducer whereas the melanin exocytosis, triggered by UV irradiation, was successfully quantified using a commercial electrode and it was found a concentration of 3 and 13  $\mu$ M melanin after irradiation for 15 and 30 min, respectively.

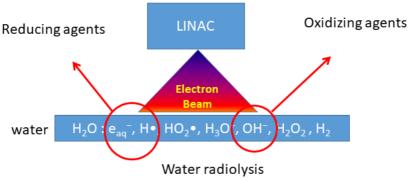
Acknowledgements: This work was supported by Romanian Ministry of Research, Innovation, and Digitalization, CNCS-UEFISCDI through projects PN-III-P4-ID-PCE-2020-1403 PNCDI III and National Research Council (CNCS) the Core Program Project PC1-PN23080101.

<sup>\*</sup>adrian.enache@infim.ro

# Electron Beam Synthesis of Iron Oxide Nanoparticles for Biomedical Applications

Nicusor IACOB<sup>1,\*</sup>, Cezar COMANESCU<sup>1</sup>, Gabriela CRACIUN<sup>2</sup>, Andrei C. KUNCSER<sup>2</sup>, Cristian RADU<sup>2</sup>, Petru PALADE<sup>1</sup>, Elena MANAILA<sup>2</sup>, Gabriel SCHINTEIE<sup>1</sup>, Daniel IGHIGEANU<sup>2</sup>, Victor KUNCSER<sup>1</sup>

Utilizing ionizing radiation in the synthesis of magnetic nanoparticles serves to decrease the metal's valence [1], thus substituting traditional chemical reduction agents that are not environmentally friendly. This process operates through water radiolysis [2], wherein water molecules undergo molecular dissociation and generate reactive and oxidative species upon exposure to gamma or high-energy electron beam (EB) radiation. The thermally activated electrons generated during the radiolysis process exhibit high reactivity with a strongly negative redox potential [3]. On the other side, oxidative species should be neutralized by specific scavengers (e.g., isopropyl alcohol). This work demonstrates the feasibility of synthesizing Fe<sub>3</sub>O<sub>4</sub> nanoparticles using a 5.5MeV EB from a linear electron accelerator. The Fe<sub>3</sub>O<sub>4</sub> nanoparticles, measuring 7-8 nm in size, were characterized using transmission electron microscopy (TEM), X-ray diffraction, Mössbauer spectroscopy, and superconducting quantum interference device (SQUID) magnetometry. Controlling the size and structural integrity of nanoparticles during EB radiolytic synthesis is crucial for harnessing the benefits of this method.



Acknowledgements: This work was supported by Core Program, component project: PN23080101 at NIMP, funded by Romanian Ministry of Research, Innovation and Digitization.

- [1] J. Belloni, Catal. Today 2006, 113, 141-156.
- [2] A. Abedini, E. Saion, F. Larki, et al., Int. J. Mol. Sci. 2012, 13, 11941–11953.
- [3] J. Belloni, M. Mostafavi, H. Remita, et al., New J. Chem. 1998, 22, 1239–1255.

<sup>&</sup>lt;sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup>National Institute for Laser, Plasma and Radiation Physics, 077125 Magurele, Romania

<sup>\*</sup>nicusor.iacob@infim.ro

# A Computational Perspective on the Fundamental Aspects of Magnetic Hyperthermia

# Andrei C. KUNCSER<sup>1,\*</sup>, Cristian RADU<sup>1,2</sup>, Ioana D. KUNCSER<sup>1</sup>

<sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

The present work tackles fundamental aspects of magnetic hyperthermia, regarded as a promising supporting therapy against various types of cancer [1].

In the case of magnetic hyperthermia, the destruction of tumor cells is accomplished by a localized heating generated by a magnetic nanoparticle system (MNP) system under the influence of an oscillating magnetic field [2]. The mechanisms of power dissipation from the MNP to the environment is related to the magnetic relaxation phenomena inside the nanoparticles [3]. The magnetic anisotropy of each MNP is an important contributing factor to magnetic relaxation.

The influence of MNP morphology and organization (Fig1) on the uniaxial anisotropy of individual entities within the system is explored. This is accomplished by computational methods, involving both micromagnetic simulations (using Object Oriented Micromagnetic Framework) and in-house Python designed software for data manipulation.

This approach aims for better insight on the magnetic relaxation phenomena in MNP systems, in the same time providing perspectives for fine tuning of the heat transfer to the tumor tissue.

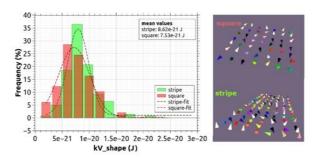


Fig. 1. Anisotropy energy distribution for MNPs in stripe (green) vs square (red) configuration.

Acknowledgements: Financial support of Romanian Ministry of Research and Innovation through project PN-III-P1-1.1-TE-2021-0273

- [1] A. Wlodarczyk, S. Gorgon, A. Radon, K, Bajdak-Rusinek, Nanomaterials 2022, 12, 1807.
- [2] A. Skumiel, J. Magn and Magn Mat. 2022, 553, 169294.
- [3] A. Kuncser, N. Iacob, V. Kuncser, Beilstein J. Nanotechnol. 2019, 10, 1280–1289.

<sup>&</sup>lt;sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

<sup>\*</sup>andrei.kuncser@infim.ro

Reliable Evaluation of Drug Loading Degree of Fe Oxide Nanoparticles by Combined Mössbauer Spectroscopy and Magnetometry

# Victor KUNCSER<sup>1,\*</sup>, Petru PALADE<sup>1</sup>, Gabriel SCHINTEIE<sup>1</sup>, Cezar COMANESCU<sup>1</sup>, Nicusor IACOB<sup>1</sup>, Luiza-Izabela TODERASCU<sup>2</sup>, Gabriel SOCOL<sup>2</sup>

Drug delivery mediated by biocompatible magnetic nanoparticles (NPs) allows the targeted internalization of specific drugs in the cells [1]. The optimal loading degree of drug molecules on nanoparticle surface as well as their corresponding release (*e.g.*, by radiofrequency magnetic field hyperthermia) is of critical interest in biomedicine.

A methodology for a reliable evaluation of the drug loading degree of magnetic Fe oxide NPs is proposed in this work. Essentially, it is based on magnetic and Mössbauer spectroscopy characterization of naked and subsequently functionalized NPs, in successive steps. The Mössbauer spectroscopy results provide primary information on the spin configuration of the Fe oxide NPs and on its specific modification at the nanoparticle surface, as induced by the presence of successive surfactant layers. This information can be intimately correlated with the contribution of the magnetic core to the total saturation magnetization in the naked and functionalized magnetic nanoparticles, respectively, the difference to the experimentally obtained magnetization of functionalized nanoparticles being correlated to the mass of successive surfactants, *i.e.* to the loading degree by biomolecules in each step of functionalization. Exemplification of this methodology in two particular cases will be provided. The two cases concern magnetite NPs firstly covered with different organic molecules (L-Cysteine and Citric Acid, respectively) for preventing a possible agglomeration and secondly loaded with drug molecules used in cancer therapy, as for example Doxorubicin [2]. Mössbauer spectra were recorded at different temperatures from 6 K to 300 K in order to investigate changes in the spin configuration

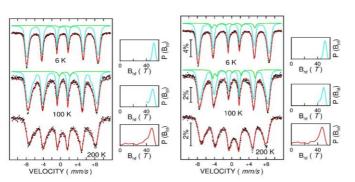


Fig.1. Mossbauer spectra collected at different temperatures on naked NPs and on NPs functionalized with L-Cysteine.

at the particle surface, as induced by the chemical interactions with the organic molecules (Fig.1). Mossbauer data were corroborated with magnetometry data collected via Zero Field Cooled - Field Cooled (ZFC-FC) saturation and

magnetization (M(H))

measurements.

By corroborating

such information subsequently obtained on naked, coated and coated-loaded nanoparticles, the loading degree with subsequent organic layers was derived and compared with much indirect and rough information obtained

<sup>&</sup>lt;sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup> National Institute for Laser, Plasma and Radiation Physics, 077125 Magurele, Romania

<sup>\*</sup>kuncser@infim.ro

by optical methods. Beside the evaluation of loading degree of Fe oxide NPs with biomolecules, the proposed methodology brings also information about the effects of the modified spin configuration at nanoparticle surface on the hyperthermia efficiency of the functionalized NPs.

- [1] V. Socoliuc, M.V. Avdeev, V. Kuncser, et al., Nanoscale 2022, 14, 4786-4886
- [2] L.I. Toderascu, L.E. Sima, S. Orobeti, et al., Nanomaterials 2023, 13, 621.

# Cytotoxicity and Biotransformation of Cerium Oxide-Iron Oxide Platform in Cells Cultures and Murine Model

# Valentin-Adrian MARALOIU<sup>1,\*</sup>, Catalina MIHALCEA<sup>1,2,\*</sup>, Cristian RADU<sup>1,2</sup>, Yuliia SHLAPA<sup>3</sup>, Anatolii BELOUS<sup>3</sup>, Aida SELARU<sup>4</sup>, Sorina DINESCU<sup>4</sup>, Cosmin MUSTACIOSU<sup>5</sup>

A platform combining two types of NPs with demonstrated capabilities provides both diagnostic capability via iron oxide (MR imaging agent) and therapeutic functionality via cerium oxide (anti-ROS capability) in one dose. This combination also allows tracking of cerium oxide delivery to the disease site and enables its biodistribution evaluation. It was demonstrated that this CO-ION platform is a good contrast agent for MRI and it has significant anti-ROS ability with good cell uptake and low cytotoxicity [1].

Vero (kidney) and Huh7 (liver) cells were incubated with initial Fe<sub>3</sub>O<sub>4</sub> and CeO<sub>2</sub> particles and CO-ION platform (25  $\mu$ g/mL and 200  $\mu$ g/mL) for 1, 2, 3 and 5 days. The evaluation of cytotoxic potential and of the potential of initial nanoparticles and CO-ION platform to induce or reduce reactive oxygen species (ROS) were done by LDH test and ROS–Glo H<sub>2</sub>O<sub>2</sub> assay respectively. Tests showed that the levels of toxicity for CO-ION platform are relatively constant and that ROS response in cells appears for higher concentrations of nanoparticles. CO-ION platform was also tested in a murine model. CRBL/6 mice were injected with a dose of 25  $\mu$ g/mL and *ex vivo* samples of liver, spleen and kidney were taken at 1, 2, 7, 15, 30, 60, 90 and 120 days after administration. Investigation showed that CO-ION platform in the administered dose didn't induce toxicity effects in the studied organs. Biodistribution and biodegradation of initial nanoparticles and CO-ION platform were investigated using Transmission Electron Microscopy techniques (CTEM, SAED, HRTEM, EDS and EELS). CTEM images (Fig. 1) show that internalized nanoparticles are distributed directly in the cytoplasm. EELS spectra (Fig. 2) demonstrate that there is no biodegradation or biotransformation of nanoparticles inside cells for up to 5 days.

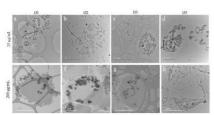


Fig. 1. C-TEM images showing Vero or Hub-7 cells internalizing CO-ION platform at different days and concentrations.

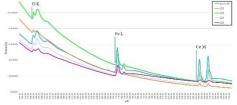


Fig. 2. EELS spectra of CO-ION platform at different days after internalization by Vero cells at 25  $\mu$ g/mL concentration.

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Reference:

[1] Y. Wu, Y. Yang, Z.P. Xu, et al.; J. Mater. Chem. B 2018, 6, 4937–4951.

<sup>&</sup>lt;sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

<sup>&</sup>lt;sup>3</sup>V.I. Vernadsky Institute of General & Inorganic Chemistry of the NAS of Ukraine, 03142 Kiev, Ukraine

<sup>&</sup>lt;sup>4</sup>Department of Biochemistry and Molecular Biology, University of Bucharest, 050095 Bucharest, Romania

<sup>&</sup>lt;sup>5</sup>Horia Hulubei National Institute for Physics and Nuclear Engineering, 077125 Magurele, Romania

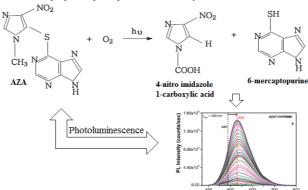
<sup>\*</sup>maraloiu@infim.ro; catalina.mihalcea@infim.ro

# Optical Evidence of Photodegradation of Azathioprine Under UV Irradiation in an Oxygen Atmosphere

# Andreea NILĂ<sup>1,\*</sup>, Ion SMARANDA<sup>1</sup>, Corina-Mihaela MANTA<sup>2</sup>, Dumitru SAMOHVALOV<sup>2</sup>, Daniel GHERCA<sup>2</sup>, Mihaela BAIBARAC<sup>1</sup>

<sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

In current life, pharmaceuticals are still considered emerging pollutants due to the lack of regulations or directives, so there is an urgent need for intelligent degradation measures. In this study, optical evidence for the photodegradation of azathioprine (AZA) under UV irradiation in an oxygen atmosphere is reported using correlated studies of photoluminescence (PL), photoluminescence excitation (PLE), UV-VIS and IR absorption spectroscopy, and Raman scattering. The photodegradation process of AZA is firstly highlighted by a PL study, which shows a 111-fold increase in PL band intensity under UV irradiation, indicating the formation of two reaction products: 4-nitro imidazole 1-carboxylic acid and 6-mercaptopurine. To enhance comprehension of this phenomenon, we study the charge transfer mechanism from AZA to the resulting phototransformation products by calculating the density of states of AZA and its reaction products. In addition, the PLE and UV-VIS absorption spectra of AZA show a gradual decrease in the intensity of the band peaking at 276 nm, which is attributed to the imidazole moiety of AZA, while a new band appears simultaneously at 346 nm due to the formation of 6-mercaptopurine. The presence of a new product is confirmed by the isosbestic point at 315 nm, which indicates the equilibrium between two absorbing species. Finally, the photoproduct of 4-nitro imidazole 1-carboxylic acid is identified by FTIR spectroscopy by showing the appearance of the C=O band after UV irradiation, while Raman spectroscopy reveals the presence of the lines corresponding to the 6-mercaptopurine photoproduct induced by UV irradiation.



**Scheme 1.** Photodegradation of AZA under UV irradiation in an oxygen atmosphere.

#### Reference:

[1] I. Smaranda, A. Nila, C. Manta, et al., Results in Physics, 2019, 14, 102443.

<sup>&</sup>lt;sup>2</sup>S.C. Sara Pharm Solutions S.R.L., 050122 Bucharest, Romania

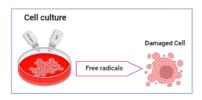
<sup>\*</sup>andreea.nila@infim.ro

# Antioxidant Properties Assessment of Spring Greens used in Traditional Romanian Green Salad

## Daniela OPREA<sup>1,2,\*</sup>, Daniel CRISAN<sup>1</sup>, Adrian ENACHE<sup>1</sup>

- <sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania
- <sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

Spring greens, often praised for their vibrant colors and fresh flavors, are also believed to contain a significant amount of polyphenolic compounds. These compounds, known for their antioxidant properties, are thought to contribute to the health benefits associated with consuming spring greens [1]. Through methods such as ultrasound-assisted acidified methanol extraction, it is aimed to quantify and evaluate the radical scavenging activity and total antioxidant capacity of these greens, shedding light on their potential health-promoting properties [2]. Antioxidant molecules have the capacity to neutralize free radicals through the process of electron transfer, whereby an antioxidant molecule is oxidized while a free radical is simultaneously reduced. The polyphenols were extracted from the selected greens using ultrasound-assisted acidified methanol technique and were evaluated by UV-Vis spectroscopy and electrochemistry to determine their antioxidant and radical neutralization capacity. The antioxidant capacity was assessed through the DPPH assay, where the absorption at 520 nm was measured spectrophotometrically. The half of the polyphenolic maximum concentration (EC50) was determined, representing the concentration required to cause a 50% reduction in the maximum absorbance of the DPPH radical. To determine the antioxidant capacity and the neutralization of half of the radicals present in the probes, two methods were employed. One method involved determining the concentration required to cause a 50% reduction in the maximum absorbance of the DPPH radical (EC50) through the DPPH assay, with spectrophotometric absorption measured at 520 nm. The other method involved assessing the highest antioxidant content by amperometry at a fixed potential of 0.3 V (vs. Ag/AgCl), while 0.7 V was chosen to estimate the total antioxidant fraction. Both methods indicated that the evaluated plants contain a high polyphenolic content with considerable antioxidant capacity and radical scavenging activity. The extracts at the EC50 concentration were also evaluated *in vitro* on cell cultures and proved their protective effect against stress agonists LPS and, inducers of oxidative stress.





#### References:

[1] L. Arfaoui, Molecules, 2021, 26, 2959.

[2] C.B. Rocha, Z.N. Caciano Pelayo, Int. J. Food Eng. 2020, 16, 20190191.

<sup>\*</sup>daniela.oprea@infim.ro

# Photoactive and Magnetoactive Nanocomposites for Biomedical Applications

Traian POPESCU<sup>1,\*</sup>, Ioana D. KUNCSER<sup>1</sup>, Valentin-Adrian MARALOIU<sup>1</sup>, Monica ILAŞ<sup>1</sup>, Arpad Mihai ROSTAŞ<sup>1,2</sup>, Alexandra-Corina IACOBAN<sup>1</sup>, Nicuşor IACOB<sup>1</sup>, Christien Oktaviani MATEI<sup>3</sup>, Tudor SAVOPOL<sup>3</sup>, Mihaela G. MOISESCU<sup>3</sup>

Magnetic hyperthermia (MHT) and semiconductor photodynamic therapy (SCPDT) represent two nanomaterial-based cancer therapeutic approaches consisting in generation of heat and oxygen radicals (ROS) into the tumor tissue, respectively [1, 2].

The herein presented studies concern biocompatible nanocomposite materials, endowed with magnetic and/or photocatalytic properties, with potential for combined MHT-SCPDT and MHT-cytostatic drug antitumor therapies. Iron oxide (Fe<sub>3</sub>O<sub>4</sub>/ $\gamma$ -Fe<sub>2</sub>O<sub>3</sub>)-TiO<sub>2</sub> nanocomposites (NCs) with core-shell structure (Fig.1 left panel) or forming solid dispersions of magnetic nanoparticles embedded in TiO<sub>2</sub> matrices have been obtained using a facile synthesis method [3]. The samples synthesized at 400 °C, containing only low amounts of weakly ferromagnetic  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> and sufficiently well-crystallized anatase TiO<sub>2</sub>, exhibited good inductive heating and ROS photogeneration properties as well as excellent cytocompatibility to human fibroblast cells, qualifying as promising candidates for antitumor applications.

Biocompatible polyhydroxyethylmethacrylate (PHEMA) hydrogels functionalized with homogeneously disperssed Fe<sub>3</sub>O<sub>4</sub>/γ-Fe<sub>2</sub>O<sub>3</sub> and TiO<sub>2</sub> nanoparticles (Fig.1 right panel) were synthesized from HEMA monomers and previously obtained active nanomaterials and their hyperthermic, photooxidation and water-soluble drug absorption properties were assessed, confirming their potential for biomedical applications.

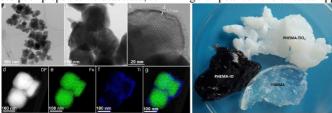


Fig. 1. Iron oxide-TiO<sub>2</sub> core-shell nanocomposites (left panel); PHEMA hydrogel and PHEMA-TiO<sub>2</sub>/Fe<sub>3</sub>O<sub>4</sub> hydrogelnanoparticle composites (right panel).

 $\label{lem:constraint} \textbf{Acknowledgements:} \ This work was supported by the Romanian Ministry of Research and Innovation through the National Core Program PN23080101, contract no. 28N/12.01.2023 and PN 23 24 01 03 contract no. 27N / 03.01.2023.$ 

### References:

[1] A.R. Lupu, T. Popescu, M. Stojanović, Chapter 2: Therapeutic use of inorganic nanomaterials in malignant disease, In: Environmental Nanotechnology – Volume 3, N. Dasgupta, S. Ranjan, E. Lichtfouse (Eds.), Springer Nature, Switzerland, 2020, pp. 47–87.

- [2] M. Sivasubramanian, Y.C. Chuang, L.-W. Lo, Molecules, 2019, 24, 520.
- [3] T. Popescu, C. Oktaviani Matei, D.C. Culita, et al., Sci. Rep. 2022, 12, 6887.

<sup>&</sup>lt;sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup>National Institute of Isotopic and Molecular Technologies, 400293 Cluj-Napoca, Romania

<sup>&</sup>lt;sup>3</sup> Department of Biophysics and Cellular Biotechnology, Carol Davila University of Medicine and Pharmacy, 050474 Bucharest, Romania

<sup>\*</sup>traian.popescu@infim.ro

# Preparation, Analysis, and Antibacterial Properties of Magnesium Doped Hydroxyapatite Suspensions

# Daniela PREDOI\*, Simona Liliana ICONARU, Steluta Carmen CIOBANU, George E. STAN National Institute of Materials Physics, 077125 Magurele, Romania \*dpredoi@gmail.com

This work aims to provide insights on the stability of suspensions of 10 MgHAp nanoparticles synthesized by an adapted chemical co-precipitation method. An adapted chemical co-precipitation method was used to obtain the magnesium-doped hydroxyapatite sample [1–2]. The magnesium-doped hydroxyapatite ( $Ca_{10-x} Mg_x (PO_4)_6 (OH)_2, x=0.1$ ) suspensions were obtained by an adapted, simple, and low-cost chemical co-precipitation at room-temperature synthesis method.

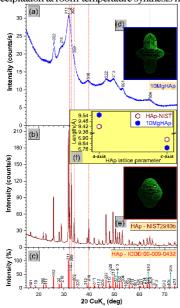


Fig. 1. XRD patterns of (a) 10MgHAp and (b) NIST SRM2910-b sample with respect to the (c) ICDD-PDF4: 00-009-0432 reference file of hex-HA. Crystallite shape as determined by MAUD modelling for (d) 10Mg-HAp and (e) NIST SRM2910-b. (f) The a-taxis and c-axis lattice parameters of 10MgHAp sample with respect to the ones determined for NIST SRM2910-b.

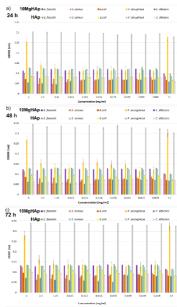


Fig. 2. The dynamics of the antimicrobial activity of 10MgHAp and HAp against E. faecalis ATCC 29212, S. aureus ATCC 25923, E. coli ATCC 25922, P. aeruginosa ATCC 27853, and C. albicans ATCC 90029 microbial cells after (a) 24 h, (b) 48 h, and (c) 72 h of incubation.

The magnesium-doped hydroxyapatite suspensions were investigated by both solid-state analysis techniques (SEM, FTIR-ATR, and XRD) and suspension-based analysis methods ( $\zeta$ -potential, ultrasound measurements, and DLS). Both  $\zeta$ -potential and ultrasound measurements showed a poor stability of 10MgHAp suspensions. FTIR-ATR and XRD measurements revealed that the obtained 10MgHAp nanoceramic had a high degree of purity (only the hydroxyapatite phase without other impurities). The uniform distribution of the constituent elements of MgHAp were demonstrated by elemental mapping EDS analysis. The 10MgHAp suspensions demonstrated antimicrobial efficacy against *P. aeruginosa*, *S. aureus*, and *C. albicans* microbial strains. The

10MgHAp suspensions could be used for the fabrication of biocompatible antimicrobial coatings of medical devices. This study highlighted the possibility of obtaining suspensions of magnesium-doped hydroxyapatite and also the evaluation, for the first time, of the behavior of these suspensions, both from the physico-chemical and the biological point of views. In addition, the influence of the 10MgHAp particles suspension on the microbial biofilm development of different microbial strains was also investigated for the first time. Further research will focus on increasing the stability of magnesium-doped hydroxyapatite suspensions to facilitate obtaining homogeneous coatings.

Acknowledgements: This work was supported by a grant of Romanian Ministry of Research and Innovation (PCCDI-UEFISCDI, project number PN-III-P1-1.2-PCCDI-2017-0062/contract no. 58/component project no. 2). References:

- [1] D. Predoi, S.L. Iconaru, M.V. Predoi, et al., Nanomaterials 2019, 9, 1295.
- [2] C.S. Ciobanu, S.L. Iconaru, F. Massuyeau, et al., J. Nanomater. 2012, 2012, 942801.

# Evaluation of Shape Anisotropy in Nanoparticles for Magnetic Hyperthermia

# Cristian RADU<sup>1,2\*</sup>, Ioana D. KUNCSER<sup>1</sup>, Andrei C. KUNCSER<sup>1</sup>

Magnetic nanoparticle systems offer innovative applications in nanomedicine, such as nano-therapeutics, multimodal imaging, targeted drug delivery, hyperthermia. Magnetic hyperthermia and temperature-controlled drug release rely on magnetic nanoparticle-mediated conversion of the alternating (AC) magnetic field energy into heat. These mechanisms depend on both the shape and size of nanoparticles as well as on the intrinsic magnetic parameters. For any nanoparticle (NP) system, among the most important pieces of physical information for scientists is information related to the morphology (size, shape, and organization) of its constituents. In this respect, an in-house software was developed and used to retrieve morphological information from electron tomography and evaluate magnetic properties.

Magnetite nanoparticles systems have been obtained by co-precipitation. The JEOL 2100 transmission electron microscope was used for preliminary sample investigations as well as for the acquisition of tomographic series. After the tomographic reconstruction was performed the 3D data was analyzed using the above-mentioned software and quantitative output information regarding the nanoparticle size, shape and orientation has been obtained. A detailed perspective on the magnetic shape anisotropy energy of the system is estimated from the shapes and sizes of the nanoparticles.

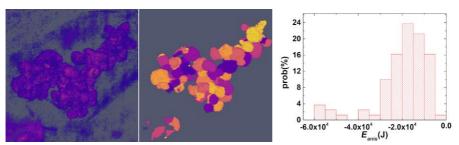


Fig. 1. Experimental tomogram data as obtained by Genfire and tomogram data after segmentation and particle separation.

Histograms showing the shape anisotropy energy density.

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- [1] A. Stanoiu, A.C. Kuncser, D. Ghica, et al., Chemosensors 2021, 9, 125.
- [2] I. Crăciunescu, P. Palade, N. Iacob, et al., J. Phys. Chem. C 2021, 125, 11132–11146.
- [3] C. Radu, I.D. Vlaicu, A.C. Kuncser, Beilstein J. Nanotechnol. 2022, 13, 590–598.

<sup>&</sup>lt;sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

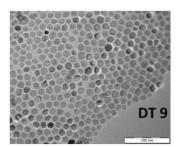
<sup>\*</sup>cristian.radu@infim.ro

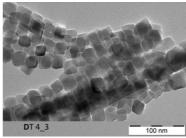
Controlling the Shape and Particle Size Distributions of Magnetic Nanoparticles Prepared by Thermal Decomposition of Organometallic Compounds

# Gabriel SCHINTEIE $^*$ , Andrei C. KUNCSER, Nicusor IACOB, Cezar COMANESCU, Victor KUNCSER

National Institute of Materials Physics, 077125 Magurele, Romania \*schinteie@infim.ro

We report a systematic study on hydrophobic and hydrophilic ultrafine magnetite magnetic nanoparticle (MNP) systems prepared by thermal decomposition of organometallic compounds. The involved range of average sizes is from 10 to 50 nm. MNPs of cubic, spherical, hexagonal, and tetrahedral shapes, which exhibit very narrow size distribution, high magnetizations and insignificant aggregation were obtained. The influence of the preparation conditions (molar ratio of surfactant mixture, time and temperature of thermal treatment) on the morphology and size of magnetite MNPs and on the magnetic properties was studied. Morpho-structural and magnetic characterizations of the prepared systems were performed by XRD, TEM, Mossbauer Spectroscopy and SQUID magnetometry. A direct correlation between the MNPs morphology and the mixture of surfactants was established. The cytotoxic effect induced by magnetic nanoparticles were investigated *in vitro* against cancer cells. Further, magnetic hyperthermia tests on the same cancer cells culture were performed and corelated with nanoparticle's magnetic properties and morphology.





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# MgB<sub>2</sub>-based Materials for Biomedical Applications

# Any-Cristina SERGENTU<sup>1,2</sup>, Petre BADICA<sup>1,\*</sup>

- <sup>1</sup>National Institute of Materials Physics, 077125, Magurele, Romania
- $^2 \textit{National University of Science and Technology POLITEHNICA Bucharest, 060042 Bucharest, Romania} \\ *petre.badica@infim.ro$

Nanomaterials show tremendous possibilities for solving many complex and urgent problems. Biomedical applications need new bioactive, biodegradable, and biocompatible materials. A novel compound showing all these features is MgB2 although this material is usually prized for superconducting properties. It has bioactivity as an antitumor and antimicrobial agent [for a review see ref. 1]. Biofilms pose a significant threat to human health and are responsible for 80% of human microbial infections. To combat them, high antibiotic doses are required, but excessive use of antibiotics and high adaptability of microbes promote the strengthening of the microbes' antibiotic-resistant behavior. Due to infections with antibiotic-resistant bacteria, only in the EU. 25,000 people die every year. Twenty new types of antibiotics were developed between 1930 and 1962, while from 1962 to the present, only two new types of antibiotics have gone into production. We have shown that MgB<sub>2</sub> is effective against both planktonic cells or biofilms of fungi or bacteria including the antibiotics-resistant ones collected from patients in the clinic. In some cases we observed a higher activity against biofilms than on planktonic cells. In vivo experiments on mice infected with E. coli have shown a decrease in the CFU/g of bacteria in liver, spleen or peritoneal liquid when MgB<sub>2</sub> is injected in the body. We also tested in vivo MgB<sub>2</sub> bulks as an orthopedic implant introduced in the femur bone of the rat model. The fracture recovered, while the implant was fully absorbed. Addition of MgB<sub>2</sub> into mouth water with chlorhexidine amplified the antimicrobial effect against oral bacteria in a synergistic manner. Delivery coatings and bulks containing as active ingredients MgB2, plant extracts, chitin and keratin were shown to be effective in healing of heavy wounds (Fig. 1). Recent results indicate that MgB2 powders modified by ultrasonication in different liquid media have higher biocompatibility opening new extended practical possibilities in the biomedical field of MgB2-based/related biomaterials.

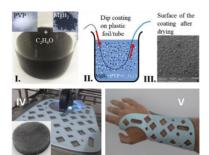


Fig. 1. Images I-III show preparation of polyvinylpyrrolidone (PVP) coatings with active components (solution preparation, dip coating, drying and coating formation on plastic foils); IV. V are stages to prepare an orthosis with active surface (3D printing and thermoforming in hot water at 80 °C) – inset presents a 3D printed sample of the orthosis surface loaded with active components in PVP. Wound healing is targeted.

Acknowledgements: This work was supported by UEFISCDI, 74-COFUND-M-ERA.NET II—BIOMB 2017, PTE 5/2020 – BIOTEHKER, Core Program PC2-PN23080202. Authors acknowledge contributions from groups at Politehnica Buc. Univ. Sci. Technol., Univ. Buc., Torino Univ., and Biotehnos SA.

#### Reference:

[1] P. Badica, D. Batalu, Green Chem. Lett. Rev. 2022, 15, 646-657.

# Effects of pH and UV Radiation on the Optical Properties of Folic Acid in Phosphate Buffer Solutions

# Ion SMARANDA<sup>1,\*</sup>, Andreea NILA<sup>1</sup>, Mihaela BAIBARAC<sup>1</sup>, Constantin SERBSCHI<sup>2</sup>

<sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

We report on the photodegradation process of folic acid (FA) in phosphate buffer (PB) solutions, evidenced by the UV-VIS absorption, photoluminescence (PL) and photoluminescence excitation (PLE) spectroscopy studies. Regardless of the pH of the PB solution, UV-VIS spectra showed a gradual decrease of the absorbance band situated at 284 nm, simultaneously with an increase in the absorbance of the band situated in the spectral range 320-380 nm, that was reduced upon exposure to UV radiation. The relative intensity of the PL band of FA, located in the spectral range 375-600 nm, depend on the pH of the PB solution. When the UV irradiation time increases up to 281 minutes, the PL intensity of FA in PB solutions with pH 6.4 and 5.4 increases. The position of the PLE band corresponding to FA, recorded under the emission wavelength of 500 nm, is changed when the pH of the PB solution varies from 7 to 5.4 and an increasing the exposure time up to 317 minutes occurs. All these changes are explained by the formation of two compounds, *i.e.* pterine-6-carboxylic acid and p-amino-benzoyl-L-glutamic acid [1]. According to the results obtained using UV-VIS, PL and PLE spectroscopy, it was found that the presence of different excipients in commercial pharmaceutical tablets has no significant effect on the photodegradation process of FA in PB solutions. Additional information on the formation of the two compounds of FA in PB solutions was reported by IR spectroscopy [2].

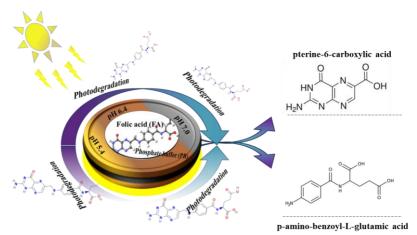


Illustration of photodegradation process of folic acid in PB solutions under UV light.

- [1] M.J. Akhtar, M.A. Khan, I. Ahmad, J. Pharm. Biomed. Anal. 1999, 25, 269–275.
- [2] M. Baibarac, I. Smaranda, A. Nila, C. Serbschi, Sci. Rep. 2019, 9, 14278.

<sup>&</sup>lt;sup>2</sup>S.C. Bioelectronic S.R.L., 100028 Ploiesti, Romania

<sup>\*</sup>ion.smaranda@infim.ro

# Ferromagnetic Shape Memory Ribbons as Potential Active Elements in Stent-Type Medical Devices

# Mihaela SOFRONIE<sup>1,\*</sup>, Felicia TOLEA<sup>1</sup>, Bogdan POPESCU<sup>1</sup>, Mugurel TOLEA<sup>1</sup>, Mihaela VALEANU<sup>1</sup>, Alexandrina NAN<sup>2</sup>, Alexander BUNGE<sup>2</sup>, Rodica TURCU<sup>2</sup>, Alexandru CHIRIAC<sup>3</sup>

1000 times higher than for the shape memory alloys.

The ferromagnetic shape memory alloys (FSMA) are interesting new materials for the manufacturing of stents due to the reversible dimension changes controlled by the application of an external magnetic field, with a major benefit in the possibility of readjusting the medical devices long after their introduction, without direct contact or a new invasive medical intervention. The Fe-Pd ( $\sim$  30 at% Pd) biocompatible FSMA undergoes the thermo-elastic and reversible structural transition - martensitic transformation - which is responsible for the shape memory effect close to room temperature, and an external magnetic field can induce deformations with moderate values, reversible and fast switchable [1]. The coexistence of the thermo-elastic and ferromagnetic features allows the shape change control under an applied magnetic field, with an actuation frequency up to

The miniaturization of the magnetic shape memory effect was achieved by an unconventional preparation technique (melt spinning), the ultra-fast solidification from the melt which allows both the freezing of the desired structural phase and the direct obtaining of variable-sized ribbons (wide or narrow), with a technological advantage in the manufacture of medical devices. In Fe-Pd-based polycrystalline ribbons, the high texture provided by the columnar microstructure, thermal treatments, and different substitutions (2 at% Ga, 3 at% Mn) shifts the structural transition from room temperature up to human body temperature, with moderate magnetically induced deformations (40 -70 ppm) in small magnetic fields (up to 0.2 T) [2]. The structural and magnetic properties were investigated by X-ray diffraction, differential scanning calorimetry (DSC), scanning electron microscopy (SEM), and magnetic (PPMS) and magnetostrictive measurements. The functionalization was performed to induce anti-thrombogenic/thrombolytic properties in the resulting ribbons and standardized thromboplastin (PTT) and prothrombin time (PT) in vitro tests were performed to evaluate the thrombogenicity of these biofunctionalized materials for a future possible monitorization of the implant in patients. The coating with poly(benzofuran-co-arylacetic acid) or olyglutamic acid polymers offers hemocompatibility and increases the implant's tolerability minimizing unwanted side effects, such as thrombus formation. In vitro, tests of standardized thromboplastin time and prothrombin time proved the thrombogenicity of these biofunctionalized materials [3]. Moreover, after coating with sulfated pectin, a heparin mimetic, the anticoagulant activity increased the activated partial thromboplastin time both in static and dynamic experiments above normal values, which proves their antithrombotic effect [4].

Acknowledgments: This work was supported by a Grant from the Romanian Ministry of Research and Innovation, CCCDI-UEFISCDI, project number PN-III-P1-1.2-PCCDI-2017-0062/contract no.58/component project no. 2, within PNCDI III and Core Program PN 18-11.

- [1] Y. Ma, M. Zink, S.G. Mayr, Appl. Phys. Lett. 2010, 96, 213703.
- [2] M. Sofronie, F. Tolea, M. Tolea, et al., M., J. Phys. Chem. Solids 2020, 142, 109446,
- [3] A. Nan, R. Turcu, C. Tudoran, et al., Polymers 2022, 14, 1397.
- [4] A. Bunge, A. Chiriac, M. Sofronie, et al., Int. J. Mol. Sci. 2023, 24, 2452.

<sup>&</sup>lt;sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup> National Institute for Research and Development of Isotopic and Molecular Technologies, 400293 Cluj-Napoca, Romania

<sup>&</sup>lt;sup>3</sup> University of Medicine and Pharmacy Grigore T. Popa, 700115 Iasi, Romania \*mihsof@infim.ro

# Copper & Gallium Co-Substituted Bioactive Glasses: Path Towards Durable Dental Implant Coatings

George E. STAN<sup>1,\*</sup>, Teddy TITE<sup>1</sup>, Adrian-Claudiu POPA<sup>1</sup>, Maria-Iuliana CHIRICA<sup>1</sup>, Cristina BESLEAGA<sup>1</sup>, George LUNGU<sup>1</sup>, Irina ZGURA<sup>1</sup>, Catalin NEGRILA<sup>1</sup>, Daniel CRISTEA<sup>2</sup>, Cristiana TANASE<sup>3</sup>, José M.F. FERREIRA<sup>4</sup>

The incorporation of therapeutic-capable ions into bioactive silica-based glasses (SBGs) is currently envisioned as an effective approach for promoting bone regeneration. In line with this perspective, the individual and combined structural and bio-functional roles of CuO and Ga<sub>2</sub>O<sub>3</sub> (in the range of 2–5 mol%) were assessed for the first time. This was accomplished by developing a series of SBG formulations derived from the FastOs®BG - 38.5SiO<sub>2</sub>-36.1CaO-5.6P<sub>2</sub>O<sub>5</sub>-19.2MgO-0.6CaF<sub>2</sub> glass parent system. The interlinked physicochemical and biological responses of BGs were evaluated to identify bio-functional triggers. The initial biological performance was examined in vitro through the quantification of Cu and Ga ion release under homeostatic conditions, cytocompatibility assays using fibroblast cell cultures, and antibacterial tests conducted against S. aureus. Copper ions were leached in comparable concentrations, ranging from 10 to 35 ppm at a BG dose of 5 mg/mL and from 50 to 110 ppm at a dose of 50 mg/mL. Conversely, the release of gallium ions ranged from 0.2 to 6 ppm, suggesting its network former role. All glasses demonstrated cytocompatibility at a dose of 5 mg/mL. Furthermore, at the same concentration, the antimicrobial effectiveness was enhanced by the simultaneous release of Cu and Ga ions. Through comprehensive evaluation, the 38.5SiO2—34.1CaO—5.6P<sub>2</sub>O<sub>5</sub>—16.2MgO—0.6CaF<sub>2</sub>—2.0CuO—3.0Ga<sub>2</sub>O<sub>3</sub> (mol%) SBG system emerged as the most promising candidate material for further development in implant coatings and bone graft substitutes. This system exhibited moderate release of Cu and Ga ions, excellent cytocompatibility, and significant antibacterial efficacy [1]. Continuing, this promising Cu and Ga co-doped SBG was utilized as the source material for producing intentionally silica-enriched implant-type thin coatings, approximately 600 nm thick, on titanium (Ti) substrates using the industrial-grade radio-frequency magnetron sputtering technology. The physico-chemical and mechanical properties, as well as the *in vitro* preliminary cytocompatibility and antibacterial performance of the alkali-free silica-rich bio-active glass coatings was further explored. The coatings were smooth (root mean square roughness < 1 nm) and hydrophilic (water contact angle of approximately 65°). Additionally, the SBG coatings demonstrated improved wear performance, with bonding strength values of ~53 MPa, Lc3 critical load values of ~4.9 N, hardness of ~6.1 GPa, and an elastic modulus of ~127 GPa. Furthermore, the Cu and Ga co-doped SBG layers exhibited excellent cytocompatibility. After 24 h, they significantly reduced the development of S. aureus bacteria by four orders of magnitude compared to control situations (i.e., nutrient broth and bare Ti). Thus, these SBGbased constructs could pave the way for high-performance bio-functional coatings with outstanding mechanical properties and enhanced biological features, such as coupling cytocompatibility with antimicrobial properties, which are highly sought after in contemporary applications [2].

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<sup>&</sup>lt;sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup>Transilvania University of Brasov, 500068 Brasov, Romania

<sup>&</sup>lt;sup>3</sup> "Victor Babes" National Institute of Pathology, 050096 Bucharest, Romania

<sup>&</sup>lt;sup>4</sup>CICECO—Aveiro Institute of Materials, Department of Materials and Ceramics Engineering, University of Aveiro, 3810-193 Aveiro, Portugal

<sup>\*</sup>george stan@infim.ro

<sup>[1]</sup> T. Tite, A.C. Popa, B.W. Stuart, et al., J. Materiomics 2022, 8, 893–905.

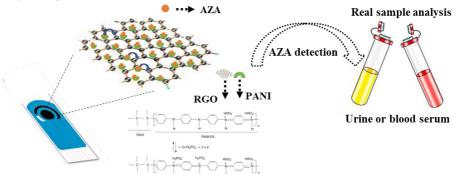
<sup>[2]</sup> G.E. Stan, T. Tite, A.C. Popa, et al., Coatings, 2020, 10, 1119.

# The Potential Applications of the Polyaniline/Carbon Nanoparticles Composites in the Azathioprine Detection

# Adelina UDRESCU\*, Mihaela BAIBARAC, N'Ghaya TOULBE, Elena MATEI

National Institute of Materials Physics, 077125 Magurele, Romania \*adelina.udrescu@infim.ro

In recently studies, a special attention was given to composites based on polyaniline (PANI) and carbon nanoparticles (i.e. carbon nanotubes, reduced graphene oxide-RGO) [1,2] for applications in pharmaceutical field. In this communication, the use of PANI/RGO modified screen-printed carbon electrodes (SPCE) for the electrochemical determination of azathioprine (AZA) is reported. AZA belongs to a class of purine analogues and immunosuppressive drugs that are used to treat diseases related to the innate immune system. The extended use of AZA, has been associated with an increased risk of cancers. Therefore, it is crucial to detect its effects accurately. The modified working electrode is a very important component of the electrochemical sensor. It is responsible for the redox reaction of the analyte molecules. The SPCE was modified with RGO sheets, both functionalized and unfunctionalized with PANI-ES [2]. An irreversible process was observed at the interface between the electrode and the electrolyte. The adsorption of AZA on the surface of SPCE modified with RGO sheets occurs through the imidazole and pyrimidine cycles of mercaptopurine, due to the formation of new  $\pi$ -  $\pi^*$  bonds between the mercaptopurine structure and the hexagonal cycles of RGO. The redox processes induced at the interface of SPCE modified with the RGO sheets functionalized with PANI-ES and electrolyte solution (AZA in phosphate buffer (PB)) lead to the generation of new positive charges on the PANI macromolecular chain. PL studies of AZA in PB have demonstrated that after ~9 hours of exposure to UV light undergoes photo-degradation processes. These results indicate the need to manipulate those electrodes in dark conditions during their use as sensor platforms for determining the concentration of AZA in biological samples [2].



Illustrative model of SPCE modified with PANI/RGO composite for the detection of AZA.

### References:

[1] M. Baibarac, A. Matea, M. Daescu, et al., Sci. Rep. 2018, 8, 9518.

[2] A. Udrescu, N. Toulbe, E. Matei, M. Baibarac, J. Nanosci. Nanotechnol. 2021, 21, 2302–2311.

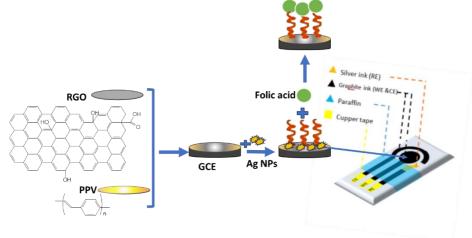
# Composites based on Reduced Graphene Oxide for Medical Applications

### Mirela VĂDUVA\* and Mihaela BAIBARAC

National Institute of Materials Physics, 077125 Magurele, Romania

\*mirela.ilie@infim.ro

Composites based on conducting polymers (CPs) and RGO have many utilization from optical and electronic devices [1], such as batteries, supercapacitors and sensors used for detection of drugs, hormones or other important biomarkers [2]. These materials display excellent mechanical, electrical, thermal, catalytic, magnetic and optical properties which cannot be obtained separately from the individual components. Even more fascinating properties are displayed when RGO based composites combined with noble metal extending their applications from catalysis, optics to nanomedicine. Composites based on RGO and CPs, such as PPV-RGO are easily synthesized using annealing method [3]. In combination with noble metal (Au, Ag) nanoparticles (NPs), which come with the effect of Surface Enhanced Raman Scattering (SERS), the new created system of SERS NPs/RGO-PPV may have as possible application folic acid detection. In addition, the studies proved that the drugs are more chemically stable in the presence of RGO sheets [4].



Possible application of RGO-CPs/Ag NPs hybrids in folic acid detection.

- [1] M. Vaduva, T. Burlanescu, M. Baibarac, Polymers 2024, 16, 53.
- [2] M. Vaduva, M. Baibarac, O. Cramariuc, Molecules 2023, 28, 135.
- [3] M. Baibarac, M. Ilie, I. Baltog, et al., RSC Adv. 2017, 7, 6931.
- [4] N. Toulbe, M. Stroe, M. Daescu, et al., Nanomaterials 2020, 10, 2238.

Composites based on Biogenic Silver, Gold, Silver Chloride and Zinc Oxide Structures as Green Multifunctional Platforms for Biomedical Applications

Irina ZGURA<sup>1,\*</sup>, Monica ENCULESCU<sup>1</sup>, Valentin-Adrian MARALOIU<sup>1</sup>, Cosmin ISTRATE<sup>1</sup>, Raluca NEGREA<sup>1</sup>, Liviu NEDELCU<sup>1</sup>, Nicoleta BADEA<sup>2</sup>, Camelia UNGUREANU<sup>2</sup>, Marcela-Elisabeta BARBINTA-PATRASCU<sup>3</sup>, Mihaela BACALUM<sup>4</sup>

Lately, the green nanotechnology emerges as a powerful tool for designing novel nanomaterials with potential applications in health area. Thus, the present work is focused on the green preparation of multifunctional mono-, bi-, tri-component structures based on Au, Ag, AgCl, ZnO by phyto-synthesis using aqueous vegetal extracts of Caryophyllus aromaticus L. (cloves buds) and Arctium lappa L. (burdock leaves). These cost-effectiveness plants were chosen considering their bioactive compounds such as essential oils, phenolic acids (chlorogenic acid, caffeic acid, cynarin, etc.), ascorbic acid, carotenoids, polyphenols, quercetin, quercitrin, arctiin, rutin, luteolin or flavonoids, these being responsible for antimicrobial, anti-inflammatory and antioxidant properties. Moreover, the burdock is one of the most popular and widespread plant in Romania being used in traditional medicine as a carminative, diuretic, depurative, antioxidant, anti-inflammatory, antibacterial, and antitubercular agent to treat many diseases (e.g., skin disorders, atherosclerosis, hepatitis, hypertension, and geriatric diseases). The morphological, structural, optical and biological properties of the prepared biogenic nanomaterials were thoroughly characterized by XRD, FTIR, UV-VIS, SEM, TEM and antibacterial activity assessments. The inorganic structures obtained in the presence of the organic compounds provided by the vegetal extracts disclose various morphologies: (i) particles (Ag, ZnO) and flowers (AgZnO) in the case of cloves extract [1] and (ii) particles (Au and AgCl), flowers and spindles (ZnO), cylinders (AuZnO), rods (AgClZnO) and particles and spindles (AuAgClZnO) in the case of burdock extract [2]. Thus, AgZnO derived from cloves is an effective antibacterial material against Staphylococcus aureus having a minimum inhibitory concentration (MIC) of 0.11 mg/mL and a minimum bactericidal concentration (MBC) of 2.68 mg/mL [1]. Due to a synergic action of all components, AuAgClZnO derived from burdock show excellent antimicrobial properties against Gram-negative bacteria like Escherichia coli and Pseudomonas aeruginosa and Grampositive bacteria like Staphylococcus aureus having diameter of the zone of inhibition (ZOI) ~20 mm (E. coli), ~27.5 mm (*P. aeruginosa*) and ~15 mm (*S. aureus*) [2]. Consequently, this green synthesis approach is an environmentally-friendly path for developing multifunctional platforms based on biogenic structures with improved antibacterial properties with potential applications in the biomedical field.

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- [1] I. Zgura, M. Enculescu, C. Istrate, et al., Nanomaterials 2020, 10, 2146.
- [2] I. Zgura, N. Badea, M. Enculescu, et al., *Materials* **2023** *16*, 1153.

<sup>&</sup>lt;sup>1</sup>National Institute of Materials Physics, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup> Faculty of Chemical Engineering and Biotechnologies, National University of Science and Technology POLITEHNICA Bucharest, 011061 Bucharest, Romania

<sup>&</sup>lt;sup>3</sup> Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

<sup>&</sup>lt;sup>4</sup> Department of Life and Environmental Physics, Horia Hulubei National Institute for Physics and Nuclear Engineering, 077125 Magurele, Romania

<sup>\*</sup>irina.zgura@infim.ro

# Nanostructured Human Serum Albumin as Drug Delivery Carrier to Cancer Cells

# Claudia. G. CHILOM¹\*, Sorina IFTIMIE¹, Adriana E. BALAN¹, Teodor A. ENACHE², Daniela OPREA¹², Monica ENCULESCU²

A folic acid-rutin -conjugated human serum albumin nanoparticles (HSA-FA-Ru NPs) drug delivery system was synthesized to deliver rutin to L929 fibroblast cell lines and HT-29 adenocarcinoma human [1]. NPs were obtained by a modified desolvation method [2]. After functionalization with folic acid, the morphological properties of NPs were analyzed by Atomic Force Microscopy (AFM) and Scanning Electron Microscopy (SEM) and the dimensions of the NPs determined were smaller than 100 nm. The time stability of the NPs was evaluated using UV-Vis spectroscopy. Therefore, these NPs represent a valuable approach for the penetration of the membrane and for cellular target. These results provided the basis for in vitro studies monitoring the effect of these NPs on L929 and Ht-29 cells. The cytotoxicity of the HSA NPs and HSA-FA-Ru NPs was evaluated by MTT assay using L929 and HT-29 cells, after 24 h of incubation with the NPs. Following treatment of both cell types with NPs, the viability of HT-29 cells was more affected than that of L929 cells, and the effect was more pronounced in the presence of HSA-FA-Ru NPs. Fluorescence microscopy showed that HSA NPs and HSA-FA-Ru NPs do not affect the nucleus and cytoskeleton of L929 and HT-29 cells, but for HT-29 cells a tendency for NPs to agglomerate on the cell surface was observed, and the effect was more evident for HSA-FA-Ru NPs. The development of HSA-FA-Ru nanohybrid is part of the efforts to improve CRC therapies and minimize severe adverse effects associated with cytotoxic drugs.

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- [1] P. Jayameena, K. Sivakumari, K. Ashok, S. Rajesh, Cells 2018, 7, 1731.
- [2] M.-E. Barbinta-Patrascu, S. Iftimie, N. Cazacu, et al., Coatings 2023, 13, 671.

<sup>&</sup>lt;sup>1</sup>Faculty of Physics, University of Bucharest, 077125 Magurele, Romania

<sup>&</sup>lt;sup>2</sup> National Institute of Materials Physics, 077125 Magurele, Romania

<sup>\*</sup>claudia-gabriela.chilom@unibuc.ro