

# nanoBalkan CONFERENCE



nanoBalkan  
2024

OCT. 28 - NOV. 01 • TIRANA, ALBANIA

## MAIN ORGANISERS



## LOCAL ORGANISERS



## nanoBalkan2024 Foreword

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On behalf of the Local, International and Technical Committees, we take great pleasure in welcoming you to Tirana (Albania) for the NanoBalkan International Conference (NB2024).

The 2nd edition of NanoBalkan is being launched following the overwhelming success of the last 3 events organised in Albania i.e. TNT2021, TNT nanoBalkan2022 and nanoBalkan2023.

This high-level scientific meeting aims to present a broad range of current research in Nanoscience and Nanotechnology as well as related policies or other kind of initiatives such as nanoAlb. The NanoBalkan2024 structure will keep the fundamental features of the previous events organised in Albania, providing a unique opportunity for broad interaction. During NanoBalkan several specific sessions on hot topics will be organised: Graphene and 2DM, nanobiosensors, nanomedicine, etc.

We are indebted to the following Institutions and Government Agencies for their financial support: Ministry of Education and Sports of Albania and Academy of Sciences of Albania.

We also would like to thank all the speakers and participants that join us in-person this year.

In addition, thanks must be given to the staff of all the organizing institutions whose hard work has helped planning this conference.

Hope to see you again in the next edition of NanoBalkan.

*NanoBalkan2024 Organising Committee*

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## Local Organisers

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# From Quantum Optics to Quantum Technologies: A Story of Gemstone and Light

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The technologies of tomorrow emerge from the science of today. This is one of the commonly used phrases to describe how scientific discoveries translate to useful technology. In the development of quantum physics, optics played a critical role from the early days at the birth of disruptive concepts to the modern era of accessing a tangible quantum world. Today, translation of curiosity-driven quantum physics to disruptive technologies is well on its way and many material platforms are under consideration for the physical implementation of useful devices. Diamond is one of many material platforms that offer promising technological roadmaps, particularly in quantum communication networks and in nanoscale sensing applications. This talk will present the journey towards near-term applications of the quantum world from the perspective of this unexpected partnership of gemstone and light.

# Tweaking 2D-materials structure for pushing the limits of electrochemical energy storage

**Aristeidis Bakandritsos**

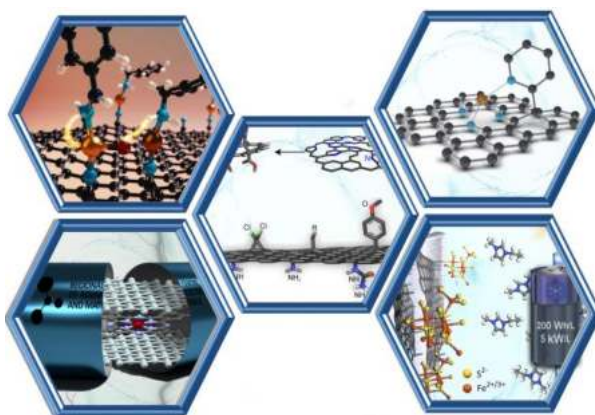
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Functionalization, doping and, in general, tweaking the form of materials (such as in graphene and other 2D materials) is fundamental for harnessing superior properties to enhance their performance in targeted applications.<sup>[1]</sup> For example, electrochemical energy storage technologies (e.g., supercapacitors and batteries) require advanced functional materials with enhanced charge transport, effective ion storage in confined spaces, integrated redox-active features and stability. Here, the synthesis of tailored graphene derivatives and the self-assembly of 2D aromatic molecular structures into nanowires are presented, and their advantageous properties as electrodes in supercaps and batteries are discussed. By leveraging the reactivity of fluorographene with nucleophiles, in-plane doped and out-of-plane covalently functionalised graphenes are obtained with high functionalization degree and selectivity.<sup>[2]</sup> The conjugation of charged molecules affords zwitterionic surfaces and  $\pi$ – $\pi$  electronic interactions, promoting ionic transport and electrochemical activity.<sup>[3]</sup> Nitrogen superdoping of graphene up to 15 at. % produces conductive, polar and dense graphene electrodes with diamond-like interlayer bonds. Such electrodes deliver ultrahigh volumetric capacitance and energy density, as demonstrated in symmetric full-cells.<sup>[3]</sup> Graphene acid, a graphene derivative with very high density in carboxylic groups, offers high redox capacity as a Li-ion anode, stemming from its abundant lithiophilic moieties, which are conjugated in a spacer-free manner on the conductive scaffold of graphene.<sup>[4]</sup> The self-assembly of 2D copper-coordinated carboxylated aromatic molecules into long nanowires leads to ultrahigh lithium diffusivity and superlithiation properties, affording anodes for lithium-ion batteries and lithium-ion capacitors with capacities surpassing 1500 mAh g<sup>-1</sup>. These properties are not observed if the same system is not in nanowire form. Through such chemical and morphological tweaking of materials, improved properties emerge, laying the groundwork for the development of materials surpassing the limits of their precursors.

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**Figure 1:** Modified two dimensional materials with improved charge transport, effective ion storage, redox-active features and stability for pushing the limits of electrochemical energy storage.



**Shimshon Belkin**

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### Abstract

Landmines and explosive remnants of war pose a global humanitarian problem which claims numerous casualties long after the conflict has ended. Current approaches for the location of landmines, such as metal detection, which require physical presence at the minefield, involve high risk to personnel; these methods are also costly, time consuming, and have a high rate of false positive results. No currently viable technology allows the remote detection of buried explosive devices. A possible solution may be provided by the use of genetically engineered microorganisms, molecularly “tailored” to emit an optical signal in the presence of trace explosives escaping for the landmine and accumulating in the soil above it. This optical signal, , can serve to generate a physical map of the mine location. We have previously described the remote detection of buried landmines using alginate-encapsulated fluorescent microbial (*Escherichia coli*) bioreporters. Since then we have modified the system to one based on bioluminescent (rather than fluorescent) bacteria, and have employed several synthetic biology approaches to significantly enhance their major performance parameters: higher signal intensity, faster response time, and lower detection threshold of the target explosives. These advanced sensor strains have been incorporated into independently deployable electronic modules that sensitively report on the presence of trace explosives under their footprint.

# Characterization of nanoparticles and other thermal breakdown products of conventional (AFFF) and replacement fluorine-free firefighting foams (FFF)

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## Abstract

Per- and poly-fluoroalkyl substances (PFAS) have emerged as a major environmental health problem of our time. Aqueous Film-Forming Foams (AFFF) are traditional firefighter foams based on PFAS and a major source of PFAS environmental pollution (1). This presentation will summarize the results of a three-year research project on barriers and incentives to adopting Fluorine Free Foams (FFFs) as safer replacements to AFFF (2). The main focus will be on the chemical composition and thermal degradation behaviour of AFFFs and FFFs replacements that can influence the fundamental physico-chemical properties relevant to human exposures: phase distribution and mobility of contaminants (gas, vapor, nano aerosol, PFAS size distribution); chemical composition (generation of free radicals, chain reactions leading to new species, including fluorinated hydrocarbons, inter-species conversions, generation of HF gas and/or acid), toxic gases (CO, SO<sub>2</sub>, NO<sub>x</sub>). These thermal degradation byproducts are biologically relevant to human exposure because they alter lung dosimetry, mode of action, and lung toxicology.

We constructed an environmental chamber testing platform suitable for characterizing thermal degradation behaviour and physico-chemical transformation of common AFFF and commercially relevant replacement FFF under controlled experimental conditions. Representative AFFF (6 of 16) and FFF (7 of 22) foam samples were burned using a standardized temperature ramp (25 °C to 800 °C) under sufficient O<sub>2</sub> conditions (21%). We characterized foam emissions with a suite of instruments that measure nano aerosol properties (size distribution and number concentration, HF gas and aerosols, toxic gases (CO, SO<sub>2</sub>, NO<sub>x</sub>), VOCs, ROS by ESR), and collected samples for subsequent chemical analysis by LC-MS/MS, NMR, SERs, and other techniques. Extensive physico-chemical characterization of the raw foams (LC-MS/MS, LC-Q-TOF MS, Raman, NMR, ICP-MS, establishes a baseline for their input chemical composition, including PFAS content and foam matrix. TDP products collected are undergoing in vitro cell culture tox testing.

The presentation will cover major findings pertaining to nanoparticles generated and their composition and discuss its implications for human health. This work was funded by the US Federal Emergency Management Agency (FEMA) Assistance to Firefighters Grant Program.

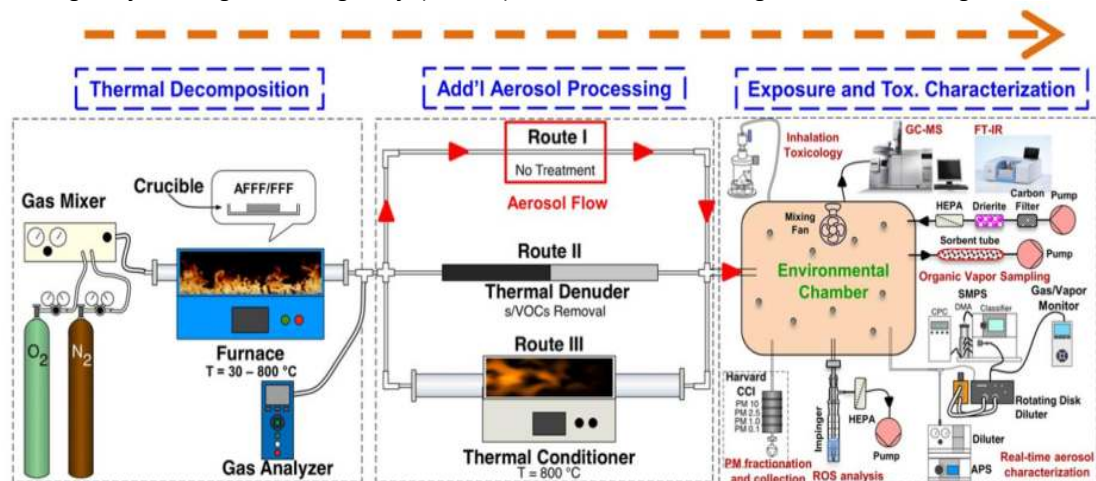


Figure 1. Schematic of the platform for comprehensive thermal decomposition studies of AFFF and FFF products

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The generation of small electric charges upon the application of mechanical stimuli to piezoelectric nanomaterials is a unique phenomenon in the context of remote stimulation of cells and tissues. Electrical cues are known to foster specific biological responses, and piezoelectric nanomaterials own the ability to act as real “nanotransducers”, thus allowing obtaining “wireless” and remote electric stimulation thanks to non-invasive excitation through mechanical sources [1].

Cancer cells are known to be sensitive to electric stimuli, and in the past years we demonstrated as piezoelectric nanoparticles activated by ultrasounds (US) can be exploited for the non-invasive and remote delivery of electric cues, enabling cell cycle arrest and apoptosis [2-3].

More recently, we proposed the exploitation of nutlin-loaded poly(vinylidene fluoride-co-trifluoroethylene) -P(VDF-TrFE)- nanoparticles stimulated with US for the treatment of glioma cells (Figure 1) [4]. Moreover, we showed that the angiogenic behavior of human cerebral microvascular endothelial cells can be inhibited by using the same approach. The anti-angiogenic effect, derived from the use of chemotherapy and chronic piezoelectric stimulation, leads to disruption of tubular vessel formation, decreased cell migration and invasion, and inhibition of angiogenic growth factors in the presence of migratory cues released by the tumor cells [5].

In a further work, we focused our attention on glioma-associated microglia (GAM), representing the largest population of “supporting” cells of the tumor microenvironment, which express the anti-inflammatory M2 phenotype, thus promoting an immunosuppressing environment that helps tumor growth. We proposed a targeted anti-glioma immunotherapy, based on pro-inflammatory modulation of the GAM phenotype through controlled and localized electrical impulses mediated by US-stimulated piezoelectric nanoparticles [6].

Concluding, the combination of chemotherapy drug delivery with chronic piezoelectric stimulation resulted in activation of cell apoptosis and anti-proliferation pathways, induction of cell necrosis, inhibition of cancer migration, reduction of cell invasiveness in drug-resistant glioblastoma multiforme cells, and even immune actions. Obtained results pave the way for the use of innovative multifunctional nanomaterials in less invasive and more focused anticancer treatments, able to reduce drug resistance in glioblastoma and trigger microglia activity against cancer cells.

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2D materials, with exceptional electrical conductivity and mechanical flexibility, are emerging systems for wearable electronics and smart textiles, offering opportunities for the seamless incorporation of electronic devices in textiles. In this talk, I will give an overview of our recent progress in integrating 2D materials with textile substrates, encompassing fibres and fabrics, for a range of textile electronics applications, including wearable sensors and energy harvesting devices, and textile environmental sensors.

We developed a versatile technique to coat common insulating textile fibres like polypropylene, polylactic acid, polyethylene, and nylon with monolayer and few-layer graphene [1,2] via Chemical Vapor Deposition (CVD). These graphene-coated fibres exhibited low sheet resistance, preserving graphene's conductivity and enabling the integration of touch-sensitive and light-emitting devices into textiles [3]. We have also used these fibres as temperature sensors in a low-voltage carbon-graphene e-textile system [4].

In the area of fabric-based wearable devices, a pivotal obstacle lies in seamlessly integrating electronics into fabrics while preserving their softness and comfort. A crucial aspect involves achieving electrically conductive coatings on textiles that adapt to the irregular and coarse structures of fabrics without compromising their properties. We introduced a straightforward, cost-effective, and highly scalable method, the ultrasonic spray coating [5]. This technique was effectively used to coat various types of textile fabrics such as meta-aramid, polyester, and nylon using water-based suspension of graphene and create fabric electrodes displaying good conductivity, and resilience to bending, compression and tension. We further demonstrated the application of these graphene conductive fabric electrodes in self-powered sensing technologies embedded in textiles [6,7]. The steppingstone for these advances is a new class of triboelectric energy harvesters able to convert presently unused sources from our living environment such as sounds and vibrations into electrical energy [8]. Due to the conformation ability of the triboelectric sensors, they were implemented on key moving parts of the human body and used to monitor biomechanical motion through electrical signals [6, 7]. The self-powered sensors demonstrate their potential for wearable bioelectronics, intelligent robotics, prostheses, and rehabilitation purposes. Finally, we demonstrated the use of graphene on fabrics for a novel textile-integrated triboelectric nanogenerator capable of sensing and harvesting low-frequency acoustic energy [8].

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In this talk, new technological and methodological approaches for interfacing the brain by photonic technologies will be shown. Tapered optical fibers are nanomachined and processed to produce optical probes and optrodes for accessing deep brain regions in animal models with spatial and temporal resolution [1-3]. These minimally invasive probes can be simultaneously exploited in both optogenetics, for manipulation of neural activity, and for recording molecular and cellular activity in fiber photometry. It will be also shown how tapered fibers can be employed in-vivo in Raman and SERS spectroscopy experiments for tumoral tissue identification and label-free neurotechnology.

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# Biomimetic Nanoparticles via Microfluidics: Advancing Precision Cancer Therapy

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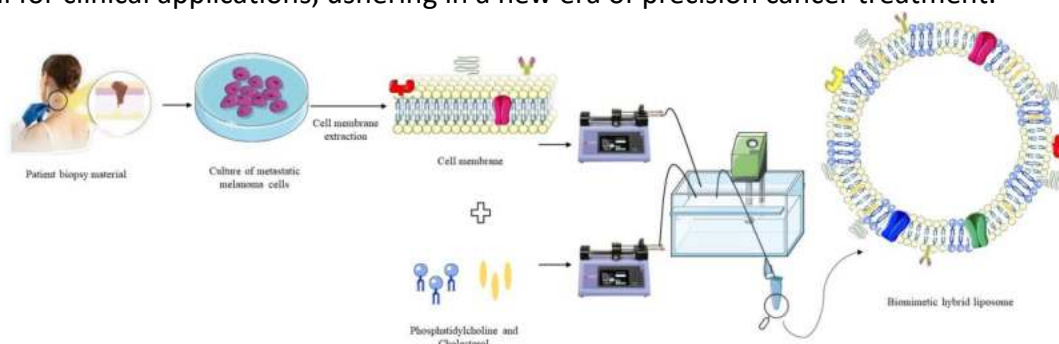
## Abstract

The precise delivery of therapeutic agents using nanoparticles (NPs) has revolutionized cancer treatment by improving diagnostic accuracy and therapeutic outcomes while reducing off-target toxicity. Recent breakthroughs in biomimetic strategies, where NPs are engineered to mimic cellular functions, offer new avenues for increasing selectivity toward tumors and their complex microenvironments (TME). [1] Biomimetic hybrid nanoparticles, particularly those combining bioactive cell membranes (CMs) with synthetic NPs, are emerging as powerful tools in cancer therapy. These nature-inspired systems enhance systemic circulation, improve targeting accuracy, and boost cellular uptake. [2]

In this keynote, I will present an innovative liposome-engineering approach that harnesses direct membrane fusion between synthetic liposomes and CMs derived from cancer cells, creating advanced hybrid liposomes. Traditional methods for fabricating biomimetic NPs, such as mechanical extrusion and ultrasonic processing, are labor-intensive and prone to inconsistencies between batches. To address these limitations, we developed a cutting-edge microfluidic sonication technique (Figure 1), which integrates active and passive mixing strategies to streamline nanoparticle production. [3] By leveraging the geometry of 3D-printed microfluidic devices for passive mixing and applying an external ultrasonic field for active mixing, we achieve efficient and consistent membrane fusion.

Through two case studies, I will demonstrate the success of our microfluidic method in fusing CMs with liposomes, with an emphasis on how active mixing significantly improves membrane fusion efficiency. Additionally, I will highlight how tumor-derived CMs enhance NP internalization in vitro, enabling homologous targeting—a key mechanism for precise drug delivery and optimized cancer therapy.

This microfluidic innovation not only simplifies the NP fabrication process but also offers new potential for clinical applications, ushering in a new era of precision cancer treatment.



**Figure 1:** Schematic representation of the microfluidic fabrication of hybrid liposome.

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## Developing Trustworthy, Causal, and Aligned Artificial Intelligence

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This talk will discuss the engineering of trust among agents, humans, and algorithms to develop practical solutions. The problems we will address include Trustworthy and Causal AI in various applications, system resilience, and creating a framework for Artificial Conscience to control AI. The trustworthiness of AI solutions is now considered essential for optimal AI usage. We have developed metrics using our trust system to evaluate AI solutions' acceptance, explainability, and fairness. Additionally, we emphasize the importance of causality as a crucial component of trustworthy AI. An essential application of Causal AI is the Manufacturing production line Root Cause Analysis. Lastly, we present our framework for Artificial Conscience, in which AI algorithms are controlled by agents who negotiate using our trust engine to produce a solution that maximizes "Artificial Feeling." This framework can be easily implemented in any AI system, incorporating metrics such as trustworthiness and causality, ultimately aligning AI with human values.

## Electrochemical CO<sub>2</sub> reduction by Boron-doped Diamond Electrodes

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Boron-doped diamond (BDD) electrodes are very attractive material, because of their wide potential window, low background current, chemical inertness, and mechanical durability.[1] In these years, we have reported several examples for electrochemical sensor applications including novel microsensing systems for in vivo real time detection of local drug kinetics.[2] Furthermore, applications for electrochemical organic synthesis[3] and electrochemiluminescence (ECL) systems[4] are also reported. Here, recent developments on electrochemical CO<sub>2</sub> reduction using BDD electrodes are presented.

In 2018, we investigated the electrochemical reduction of CO<sub>2</sub> in a flow cell using BDD electrodes. The faradaic efficiency (FE) for the production of HCOOH was as high as 94.7%. Furthermore, the selectivity for the production of HCOOH was more than 99%. The rate of the production was increased to 473  $\mu\text{mol m}^{-2}\text{s}^{-1}$  at a current density of 15  $\text{mA cm}^{-2}$  with a FE of 61%. The FE and the production rate are almost the same as or larger than those achieved using Sn and Pb electrodes. In addition, the stability of the BDD electrodes was confirmed by 24 hours operation.[5]

Then, in 2019, we were able to control the selectivity and efficiency with which carbon monoxide (CO) is produced by optimizing certain parameters and conditions used in the electrochemical process with BDD electrodes, such as the electrolyte, the boron concentration of the BDD electrode, and the applied potential. With a BDD electrode with 1% boron used for the cathode and KClO<sub>4</sub> for the catholyte, the selectivity for producing carbon monoxide was high. On the other hand, with a BDD electrode with 0.1% boron used for the cathode and KCl for the catholyte, the production of formic acid was the most evident. *In-situ* ATR-IR measurements during electrolysis showed that CO<sub>2</sub><sup>•-</sup> intermediates were adsorbed on the BDD surface in the KClO<sub>4</sub> aqueous solution. Here, switchable product selectivity was achieved when reducing CO<sub>2</sub> using BDD electrodes.[6]

Recently, in order to operate on a large scale for industrial applications, an intermittent flow cell system was presented. A stop-start motion of the flow conditions in the intermittent cell was created using a piston pump, and this considerably increases the rate of electrochemical conversion of CO<sub>2</sub> to HCOOH compared to a continuous flow system.[7] Furthermore, we found that an initial electrochemical CO<sub>2</sub> reduction reaction could significantly improved the reaction current and Faradaic efficiency of the CO<sub>2</sub> reduction on BDD electrodes.[8] The effect is referred to as the “self-activation” of BDD. Here, the mechanisms and the effect of self-activation is discussed.

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# Recent electrochemical biosensors with nanomaterials based applications: Biointeractions to Diagnostics

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## Abstract

Biosensors are analytical tools developed for sensitive and selective detection of different analytes; nucleic acids, proteins, drugs and pathogens [1-4]. The fields of genomics, biomedical diagnostics, proteomics, and drug discovery may be greatly impacted by the development of advanced biosensors based on nanomaterials because of the advantages of numerous nanomaterials with distinct mechanical, optical, electrical, and catalytic capabilities [2,3,5,6].

Different nanomaterials including carbon based nanomaterials, metallic nanoparticles and their nanocomposites with conductive biopolymers and numerous biomaterials have been applied for design and development of advanced electrochemical biosensors [2,3,7-12].

In order to study sequence-selective nucleic acid hybridization and as well as the interaction of nucleic acids with drugs, proteins, and DNA-targeted compounds, electrochemical nucleic acid biosensors combine the intrinsic specificity of biorecognition reactions with the high sensitivity of physical transducers. Recent applications of electrochemical biosensors based on nanomaterials have been overviewed herein, and discussed along with their future directions.

## Acknowledgements

Arzum Erdem Gürsan express her gratitudes to the Turkish Academy of Sciences (TÜBA) as the Principal member for its partial support.

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## **Wearable reconfigurable metamaterials and origami inspired implantable sensors for human-machine interfaces**

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Although not known widely, the field of soft robotics was born out the research in microfluidics which developed the initial methods for transport of fluids (liquids or gasses) along micron or millimeter-sized channels. We have recently discovered that when silicone-based millifluidic devices are worn as sleeves, they can be pressured with gasses to change their material properties, including their geometry and hardness acting as a metamaterial. We have exploited this phenomenon to build wearable devices that can be used in prosthetic sockets as an interface to improve the use and comfort of prosthetic limbs and tested this idea in human trials. Our research also extends beyond wearable robotics. We have been developing flexible origami-inspired implantable sensors that can be inserted into the body with a syringe and unfold like a satellite in orbit to allow minimally invasive physiological monitoring of biometrics from within the body.

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The future of biology and medicine is poised at the intersection of engineering, chemistry, nanotechnology, and materials science. Notably, the realms of micro/nano-scale technologies and biomedical engineering have undergone remarkable growth and advancement in the past decade. The integration of cutting-edge technologies at the micro- and nano-scale—termed as "disruptive innovation," presents tremendous opportunities to address unmet needs and overcome key challenges in the fields of biology and medicine. In this talk, Dr. Fatih Inci explores state-of-the-art micro- and nano-scale technologies as precise solutions to improve human health and beyond. In this context, the platforms developed in his lab manipulate biomolecules, cells, cell dusts (extracellular vesicles: EVs), and pathogens in small volumes. Among biomarkers focused on by his team, EVs emerge as crucial carriers of information in cellular communication. Initially perceived as artifacts or cell debris, EVs are now recognized for their essential roles in the development and propagation of various diseases, as well as taking serious roles in disease diagnosis and therapeutics in precision health. However, isolating these nano-sized entities in a size-dependent manner presents a significant challenge in EV research. Conventional methods are often costly, prone to the loss of differently sized EVs or susceptible to contamination, thereby compromising the quality of subsequent investigations. His team's approach harmonizes microfluidics and biosensing strategies to isolate and identify EVs from clinically relevant specimens. This development establishes a diagnostic and screening scheme for point-of-care settings, enabling individuals to easily self-monitor their health status for precision health applications. Detecting these minuscule yet impactful EV markers represent not only a game-changer in medicine, but also opens up new avenues for precision health and clinical management.



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## Revolutionizing Indoor and Outdoor Photovoltaics with 2D Materials: Boosting Efficiency, Stability, and Scalability

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The advancement of 2D materials-based photovoltaic (PV) technologies, including organic photovoltaics (OPVs) and perovskite solar cells (PSCs), is significantly propelling progress in both indoor and large-scale outdoor solar energy applications. The IntoPV project is pioneering OPV cells tailored for indoor environments, emphasizing enhanced efficiency under various lighting conditions and improved long-term stability. By integrating Transition Metal Dichalcogenides (TMDs) such as MoS<sub>2</sub>, MoSe<sub>2</sub>, WS<sub>2</sub>, and WSe<sub>2</sub> as hole transport layers (HTLs) in OPVs, the project leverages these materials' unique optical and electronic properties. Through advanced photophysical characterization and innovative fabrication techniques, including liquid-phase exfoliation and spray coating, we demonstrated that MoS<sub>2</sub>-based HTLs match or surpass traditional materials like MoO<sub>3</sub> in inverted structures, achieving high power conversion efficiency (PCE) and exceptional stability under both artificial indoor light and solar illumination. Further exploration of MoS<sub>2</sub> and WS<sub>2</sub> as HTLs in standard OPVs led to significant performance enhancements, with WS<sub>2</sub> achieving a remarkable PCE of 28.9% under dim indoor light, outperforming traditional materials like PEDOT. This PCE improvement, coupled with an enhanced fill factor (FF) and short-circuit current (J<sub>sc</sub>), is attributed to WS<sub>2</sub>'s superior surface coverage on indium tin oxide (ITO) and reduced recombination losses. The optimized OPV devices also demonstrated excellent stability, retaining 86% of their initial efficiency after 1,000 hours in ambient air. These findings underscore the potential of TMDs in advancing OPVs for practical applications, particularly in low-energy electronic devices like those powering the Internet of Things (IoT), where consistent performance under dim indoor lighting is crucial.

Simultaneously, substantial progress has been made in scaling up perovskite solar technology for outdoor use. The development of large-area perovskite solar modules (PSMs) integrated with 2D materials such as graphene and functionalized MoS<sub>2</sub> culminated in the creation of GRAPE (GRAphene-PErovskite) solar panels. The 2D materials enhance charge dynamics at the interfaces and protect the perovskite layer from environmental factors like oxygen, moisture, and metal ion migration. In this context, five square meters of perovskite PV panels were installed at a solar farm on the HMU campus in Crete for outdoor field testing. The solar farm's energy output was continuously monitored using custom-built maximum power point trackers, correlating the farm's performance with environmental conditions recorded by a weather station. The solar farm achieved a peak output exceeding 260 W, demonstrating the scalability of the proposed system. During the twelve-month monitoring period, the energy output exhibited a 20% decline in performance after eight months of operation (T<sub>80</sub> of 5,832 h). Further analysis revealed that high temperatures, solar irradiance, moisture, and oxygen infiltration, due to lamination failure, were primary factors in the degradation of the panels. Unique light-soaking behaviours were also observed before and during the degradation process, affecting power output. The study showed that the perovskite modules developed optical defects over time, illustrating the detrimental effects of lamination failure. Despite these challenges, the data indicated that perovskite panels hold significant promise for outdoor operations in high-temperature, high-irradiance environments. These efforts underscore the transformative potential of 2D materials in both indoor and outdoor PV applications. The use of TMDs and graphene-based materials not only enhances the efficiency and stability of PV devices but also supports the scalability of these technologies from lab-scale prototypes to real-world solar farms. This research paves the way for the broader commercial adoption of 2D materials-based photovoltaics, offering sustainable and efficient energy solutions across diverse applications.

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Blindness poses a growing global challenge, with approximately 26% of cases attributed to degenerative retinal diseases. While gene therapy, optogenetic tools, photosensitive switches, and retinal prostheses offer hope for vision restoration, these high-cost therapies will benefit few patients. Understanding retinal diseases is therefore key to advance effective treatments, requiring *in vitro* models replicating pathology and allowing quantitative assessments for drug discovery. The key to increasing our understanding of outer retinal disease mechanisms is the establishment of *in vitro* experimental models of the human retina that replicate disease pathology and permit the quantitative assessment of parameters for drug discovery. Relying solely on experimental animals is no longer sufficient, as differences in physiology and disease mechanisms often exist between these and humans. Pluripotent stem cells (PSCs) offer great promise in this respect. The ground-breaking study by Sasai and colleagues in 2011 demonstrated the replication of retinal development in three-dimensional (3D) culture conditions using murine embryonic stem cells (ESCs) [1, 2]. Subsequently, this achievement was replicated using human ESCs and induced pluripotent stem cells (iPSCs) and the resulting cellular organisations are now routinely referred to as retinal organoids - 3D laminated structures comprising all essential retinal cell types, faithfully recapitulating retinal development and function, including interconnected and light-sensitive photoreceptors [3]. The capacity for self-assembly of a stratified replica of the retina is of enormous value as this allows us to interrogate cellular interconnectedness – an aspect impossible with isolated retinal cells. This proves particularly valuable for assessing the impact of candidate drugs on the overall retina, so there is considerable excitement about the potential utility of retinal organoids for this purpose. However, it is crucial to acknowledge the artificial nature of these constructs, marked by several limitations, notably the absence of vascular input and immune system influence. While limited types of immune cells can be introduced, currently restricted to microglia, incorporating an RPE layer and integrating replicas of Bruch's membrane (BrM) and the choroidal vasculature demand further study. In this talk I will discuss the progress achieved in the last two decades concerning the differentiation of human PSCs into retinal organoids, focusing on their applications in disease modelling for age-related and inherited retinal diseases, the evaluation of new therapies, as well as contributions to drug repurposing, biomarker discovery, and toxicity assessment.

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## Clip-off Chemistry: Synthesis by Bond Cleavage

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Historically, innovations in synthetic methods and reactions have changed the way scientists think about designing and synthesizing materials and molecules. Indeed, novel synthetic methods not only unlock access to previously unattainable structures, but also inspire new concepts as to how we design and build materials to address global social, economic and industrial needs. In this talk, I will present the concept of bond breaking as a new synthetic methodology that we have named Clip-off Chemistry. Unlike most state-of-the-art synthetic approaches, which use bottom-up strategies to link atoms and molecules through the formation of new bonds, Clip-off Chemistry is based instead on the selective cleavage of existing bonds in molecules and materials, providing precise spatial control over bond cleavage. Therefore, Clip-off Chemistry represents a new synthetic methodology, whereby the programmed selective disassembly affords new molecules and materials. This disassembly occurs at the molecular level through a chemical reaction; in a first approach, through ozonolysis, a gas/solid reaction that enables cutting of constituent organic molecular building blocks or linkers via direct cleavage of their alkene bonds. In this talk, I will show the principles of Clip-off Chemistry, and the first examples of structures and molecules synthesized through controlled bond fission in porous reticular materials (*i.e.* MOFs, macrocycles and cages).

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Nanoformulations offer multiple advantages over conventional drug delivery, enhancing solubility, biocompatibility, and bioavailability of drugs.<sup>1</sup> Following systemic delivery nanocarriers must deliver encapsulated drugs, usually through nanocarrier degradation. A premature degradation or the loss of the nanocarrier coating may prevent the delivery of drugs to the targeted tissue. Despite their importance, stability and degradation of nanocarriers in biological environments are seldom studied in literature. Understanding fate and how nanomaterials change in biological matrixes is also fundamental for their toxicological evaluation as changes in nanoparticles surface or release of ions or molecules can induce toxicological endpoints. In biological fluids the presence of proteins from the media leads to the formation of a protein coating around nanoparticles, the protein corona. This corona gives a different biological entity to the nanocarrier surface and may alter toxicological endpoints. One of the main areas of research in our group in the last years has been the study of the fate of nanomaterials, aiming to understand how their properties change in biological environments. In this presentation issues related to the biological fate and stability of nanocarriers in biological matrixes will be discussed: the interaction of the nanocarriers with proteins, the biodistribution of the nanocarriers, their biological fate, the kinetics of drug release in vivo and the stability of the core and surface coating of the nanocarriers as well as the formation of protein corona in vivo. Different types of nanomaterials will be discussed: poly lactic co glycolic nanoparticles<sup>2</sup>, polymersomes<sup>3</sup>, polyplexes for siRNA delivery<sup>4</sup>, and mesoporous silica nanoparticles<sup>5</sup>. We will make use of Positron Emission Tomography and Single Photon Emission Tomography to study the biodistribution of nanocarriers, the stability of surface coatings and nanocarrier dissolution, and stability of hard and soft protein coronas<sup>6</sup>, making use of advanced radiolabeling strategies.

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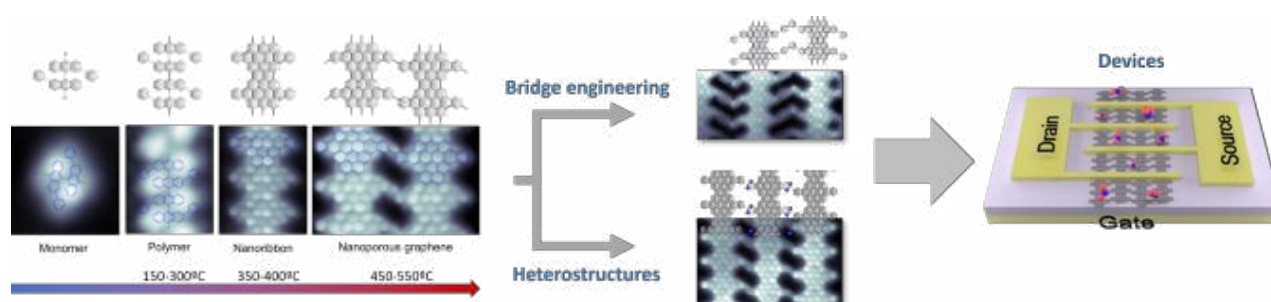
Bottom-up nanoarchitectonics has shown remarkable capability in designing nanomaterials with atomic precision. A notable demonstration of this concept is the surface-assisted synthesis of graphene-based nanostructures, where structural parameters are basically designed à la carte. However, despite significant progress in synthesizing one-dimensional homostructures, advancing towards greater structural and compositional complexity presents significant challenges. In this presentation, I will discuss different strategies that we have developed to synthesize porous graphene nanoarchitectures. All are based in a sequential method where we first grow 1D building blocks (nanoribbons), to subsequently couple them laterally [1]. This sequential method allows us to tune the atomic structure [2] and chemical composition [3] of the pores, with the possibility to realize nanoarchitectures that can be simultaneously conceived as porous membranes and ultranarrow lateral heterostructure superlattices [4].

I'll start introducing the synthesis and atomic scale characterization of different type of porous nanoarchitectures, and conclude presenting our progress towards the transfer of the nanoarchitectures onto insulating substrates in order to measure properties without the influence of the metallic substrate, and more importantly, fabricate devices.

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## Figures



**Figure 1:** Synthetic route for different porous graphene nanoarchitectures, and schematics of a field-effect transistor gas sensor fabricated with the nanoarchitectures.

# Engineering Graphene Derivatives through Tailored Functionalization for Sensing Applications

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## Michal Otyepka

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Graphene is renowned for its exceptional conductive and mechanical properties, making it highly suitable for a variety of sensing applications. However, its chemical inertness poses significant challenges for precise lattice modification, often necessitating harsh processing conditions. Direct functionalization methods yield graphene derivatives like graphene oxide, but these materials are typically non-conductive and chemically complex, which greatly limits their effectiveness in electrochemical sensing applications.

Fluorographene (FG) chemistry offers a promising solution to overcome graphene's low reactivity by enabling the scalable synthesis of graphene derivatives under mild and controllable conditions [1,2]. This approach allows for the production of both single and double-sided functionalized graphene derivatives with tailored chemical moieties that are homogeneously distributed across the graphene lattice. Furthermore, the degree of functionalization can be precisely controlled, providing a broad scope for customization [3].

The graphene derivatives produced through FG chemistry are directly applicable to a wide range of electrochemical sensing applications. Tailoring the chemical function together with degree of functionalization leads to efficient material suitable for temperature sensing without humidity interference [4]. The chemical functionalities facilitate also conjugation with biocomponents, which is advantageous for the construction of biosensors [5,6]. Additionally, the lateral size of the individual flakes makes these processed graphene derivatives suitable for inkjet printing technology. Recently, the fabrication of fully inkjet-printed electrodes applicable to electrochemical sensing has been demonstrated [7].

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# Nanomaterial Embedded Molecularly Imprinted Polymer Sensors for The Pharmaceutical and Biomedical Assay: Recent Developments and Future Prospects

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Molecular imprinting technology forms molecularly imprinted polymers (MIPs), which is a creative method that enables synthetic biorecognition gaps to imitate real biological derivatives like antibodies, receptors, enzymes, etc. After removing the target analyte, synthetic cavities enable the recognition and selective rebinding of the template. In this case, molecular imprinting technology offers biosimilar receptors with higher specific affinities and better stability than natural receptors and biomolecules [1]. Molecularly imprinted polymer (MIP) is illustrated as an analogue of a natural biological antibody-antigen system.

Although stable and durable MIPs seem relatively easy to create to achieve maximum efficiency, some optimization parameters should be considered, such as appropriate functional monomer and crosslinker and optimal ratios between functional monomer, template, and crosslinker [2]. The optimization process can vary based on the polymerization technique (electropolymerization, photopolymerization, and thermal polymerization). In addition, the structure of the polymeric matrices and the type of bond contact between the template and the polymer are two important factors in MIPs. It was reported that template monomer interactions are realized through non-covalent interactions such as van der Waals forces, hydrogen bonds, and dipolar interactions [1, 2]. Among them, MIP-based electrochemical sensors have a significant place because, with MIPs, it is possible to overcome the lack of selectivity issue in electrochemical sensors.

Nanotechnology has become very popular in the sensor fields. It is thought that the utilization of such technologies and the use of nano-sized materials could have beneficial effects on the performance of sensors. Nano-sized materials have been shown to have several novel and interesting physical and chemical properties.

Nanomaterials, famous for their prominent electron transfer capacity and specific surface area, are increasingly employed in modifications of MIP sensors. Unlike traditional electrochemical sensors, nanomaterials-based MIP sensors have excellent sensing and recognition capabilities. MIP is an appropriate substrate for electrochemical sensors owing to its binding sites, which match the target analytes' functional groups and spatial structure. However, the irregular shapes and slow electron transfer rate of MIP limit the sensitivity and conductivity of electrochemical sensors.

Nanomaterial-based MIP sensors and miniature electrochemical transducers have proven their practicality by successfully detecting target analytes in situ. Their superior chemical and physical stability, low-cost manufacturing, high selectivity, and fast response have made nanomaterial-based MIPs an exciting field of research. The studies on electrochemical nanomaterial-based MIP sensors to identify pharmaceuticals, heavy metals, hormones, enzymes, and biomarkers have shown promising results. These sensors have been successfully used in biological fluids (serum and urine samples) and pharmaceutical samples, demonstrating their real-world applicability.

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# Generation of Nanomaterials via Spark Discharge: A Rapid, Environmentally Friendly, and Versatile Method for In-Situ Modification of Electrode Surfaces

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Spark discharge is emerging as one of the most promising physical methods for producing various types of nanomaterials, including metals, semiconductors, alloys, or carbon. This process occurs without the need for liquids, chemicals, or templates. It relies on the application of an electric field capable of generating an electric discharge when two conductors, connected to an external power supply, are brought close together. In the context of electrochemical (bio)sensing applications, one of the conductors is the sensing (working) electrode, while the other acts as the source of modifying material, such as a metal, alloy, or carbon (referred to as the electrode tip).

During the dielectric breakdown process, free electrons and ions are produced from ionized molecules of air constituents. These particles then bombard the sparked electrodes. The heat generated by the flow of electricity leads to the formation of air plasma and vaporized particles from each electrode material at the closest points between the conductors. After a natural cooling process, the vaporized material solidifies and deposits onto the surface of the electrodes.

This technique offers a straightforward method for generating template-free (nano)materials of high purity. It allows for the in-situ modification of sensing electrodes, resulting in sensors with enhanced detection capabilities and a wide range of applications. Sparked (single or mixed) metal or graphite nanomaterial-modified electrodes can be prepared on demand, even on-site, within seconds, using a completely green and solution-free method that only requires the respective metal/alloy/carbon wire and a power supply. Data on the generation of bismuth, copper, nickel, and alloyed copper/nickel, tin, gold, iron, molybdenum, carbon, and cobalt sparked nanomaterials on screen-printed, 3D-printed and laser scribed graphite electrodes as well as the analytical utility of the resulting sensors will be presented [1-17].

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# Nano structuring Molecular Glasses via Anomalous Melting and Wrinkle Formation

(Calibri 15)

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When small organic molecules are deposited from vapor under optimized conditions, they can form thin film glasses with exceptional properties. These materials, known as ultrastable glasses (UG), exhibit enhanced stability and melt at temperatures well above the glass transition temperature ( $T_g$ ) of the ordinary glass [1]. Thin film UGs transition into liquid through a surface-initiated growth front. If the surface is adequately capped by higher  $T_g$  material, melting occurs through a heterogeneous process that resembles nucleation and growth. This characteristic enables the creation of glasses with nanoscale regions that have varying stabilities and glass transition temperatures. We have extensively explored this anomalous transformation by nanocalorimetry [2,3] and real-time AFM imaging [4]. Additionally, molecular orientation can be tuned during growth, offering a way to control polarization in glasses containing dipolar molecules [1,5]. These combined properties open possibilities for improving organic light-emitting devices [6], enhancing bulk heterojunction photovoltaic cells or designing new nanostructures with unique functionalities. I will also discuss strategies and initial efforts to induce localized wrinkling in thin film ultrastable glasses, as well as the development of a nanostructured glass.

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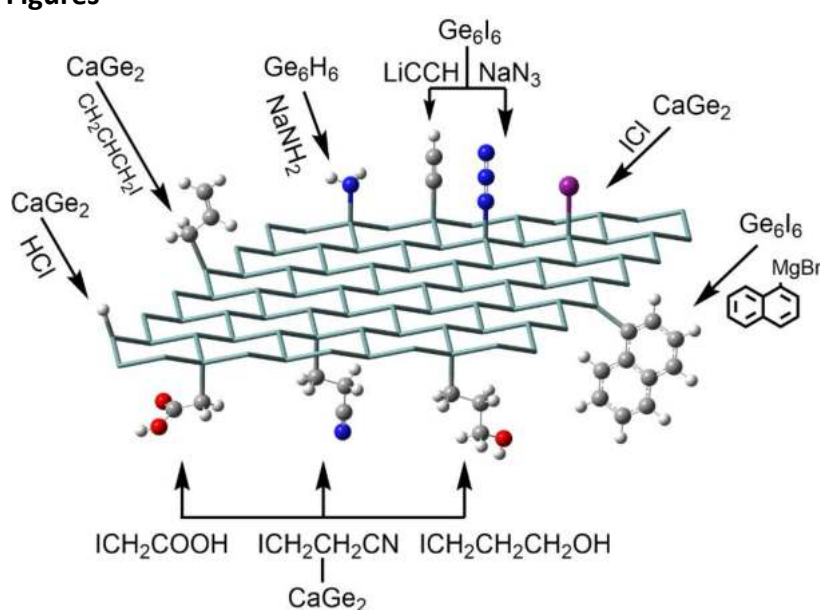
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The Xenes are rapidly developing family of monoelemental 2D materials. The chemistry of graphene as well as other monoelemental materials from group of tetrels and pnictogens will be shown in detail describing various strategies for its synthesis and chemical exfoliation. The differences between the exfoliation of pnictogens and tetrels will be described using chemical and mechanical exfoliation methods. [1] In addition, the methods for the synthesis of all main group of 2D compounds and techniques of crystal growth will be presented.

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### Figures



**Figure 1:** The possible functionalization methods for 2D silicon and germanium.

# The Role of Paper-Based and Electrochemical Biosensors in Multiplexed Diagnostics

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Multiplexed testing systems are revolutionizing modern diagnostics by providing significant advancements in detection speed, sensitivity, and specificity. This presentation explores the forefront of these innovations, focusing on the development and application of paper-based and electrochemical biosensors. Paper-based diagnostic systems are increasingly recognized for their affordability and ease of deployment in point-of-care settings, especially in resource-constrained environments. [1, 4] These platforms utilize microfluidic technologies to simultaneously detect multiple analytes, thereby enhancing their utility in diverse diagnostic scenarios. [2] Additionally, the simplicity of their design allows for easy integration with various detection methods, including colorimetric and fluorescence-based assays, making them highly versatile tools in diagnostics. Electrochemical biosensors, on the other hand, offer exceptional sensitivity and the capability for real-time monitoring. By integrating advanced materials such as carbon-based nanostructures and metal-organic frameworks, these sensors have achieved remarkable specificity in detecting low-abundance biomarkers, enabling the simultaneous detection of multiple analytes, which is crucial for comprehensive disease diagnostics and monitoring. [3, 5] Moreover, their adaptation into multiplexed detection platforms expands their application in both clinical diagnostics and environmental monitoring, offering unparalleled precision and reliability. This lecture will provide a detailed evaluation of the current state and future directions of multiplexed testing systems, and the challenges faced in integrating these technologies, particularly highlighting how the convergence of paper-based and electrochemical biosensors is setting new standards in diagnostic accuracy and efficiency.

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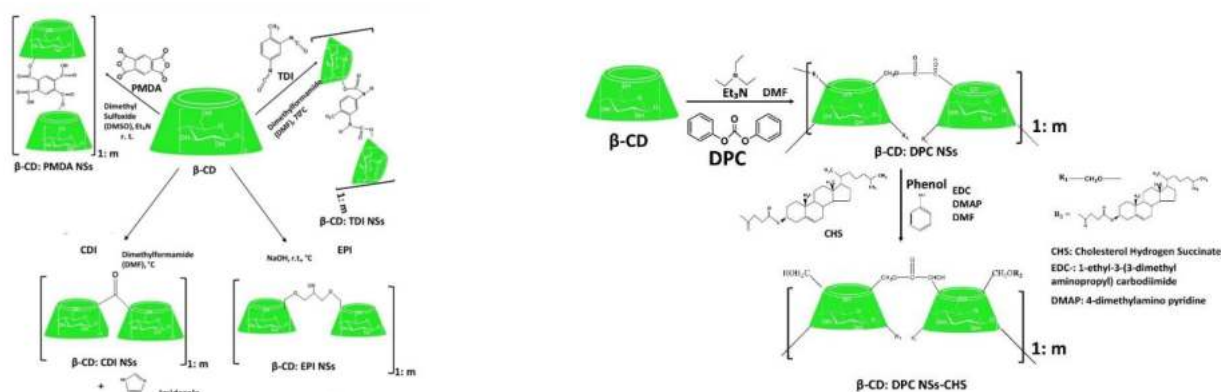
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Nanotechnology stands at the forefront of 21st-century innovation with high applicability of the materials at the nanosize scale in many industrial fields such as electronics and ICT, energy, agriculture, environment and nanomedicine. Cyclodextrin-based polymers (CD-based polymers) are among the most promising nanocarriers that combine biocompatibility with versatility, making them subjects of extensive research and application across various fields. Over time, CD-based polymers have evolved from simple reaction processes to more complex methodologies, reflecting a notable trend towards greener synthesis methods. These nanocarriers exhibit remarkable properties to enhance the solubility, bioavailability, and stability of various compounds, making them ideal candidates for drug, protein, gene, natural compounds, and gas delivery. The versatility of CD-based polymers extends beyond healthcare, impacting fields such as chemistry, environment, agriculture, cosmetics, biotechnology, batteries, and additives for the preparation of mixed matrix membranes for gas separation [1, 2, 3]. Various synthetic conditions, organic solvents, water or natural deep eutectic solvents (NADES) are utilized to obtain both crosslinked and branched CD-based polymers. Interesting results were obtained using active carbonyl compounds such as 1,1'-carbonyldiimidazole, diphenyl carbonate, organic dianhydrides, polycarboxylic acid etc., as effective cross-linking agents. The synthesized materials demonstrated excellent safety, stability, biodegradability, biocompatibility, and effective complexing properties. By varying the cross-linking agent or cyclodextrin type, the channels between cyclodextrin molecules can be adjusted, influencing the porous network formation and affecting both complexation and solubilizing ability. This research paves the way to tailor nanocarrier systems with the prospect of increasing their exploitation in countless industrial applications.

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**Figure 1:** Evolution of CD-based polymer synthesis over successive generations [3].



# Single Atom Engineering with Graphene towards Applications in Catalysis, Environmental Technologies and Medicine

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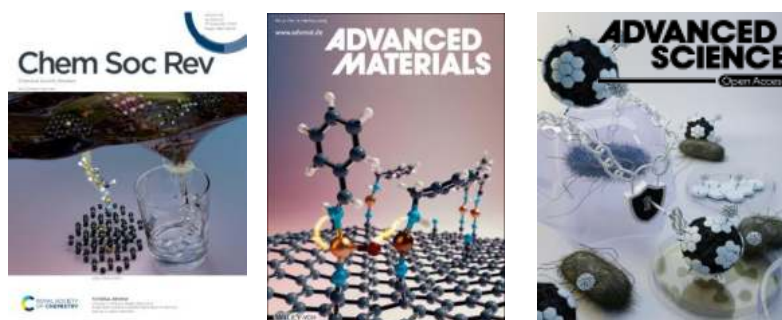
Single atom engineering is an emerging field of materials science allowing to entrap single metal species in suitable supports thus achieving unprecedented properties in various applications including catalysis, energy, medicine or environmental technologies [1,2]. The main challenge lies in the development of suitable reactive supports allowing tunable metal coordination with controllable local environment, valence state and loading of single atoms. Among various supports, the use of pristine graphene is limited due to its chemical stability and restricted possibilities of tailored functionalization for single metal embedding.

Here, we show the unique applicability of well-defined graphene derivatives, graphene acid and cyanographene [3], for the development of advanced single-atom materials. Among catalytic applications, we will report linear structure single-atom gold(I) catalyst for dehydrogenative coupling of organosilanes with alcohols [4], and mixed valence Cu(I)/Cu(II) single atom catalyst for the oxidative coupling of amines and the oxidation of benzylic C-H bonds toward high-value pharmaceutical synthons [5].

The huge potential of single atom engineering in medical technologies will be demonstrated with the development of graphene supported silver- and manganese-based antimicrobial materials overcoming the bacterial resistance [6,7]. Finally, we will show the applicability of graphene acid and single-atom materials in water treatment technologies including heavy metals removal and antibacterial treatment [8].

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**Figure 1.** Representative cover arts of publications demonstrating the use of single atom materials in environmental technologies [2], catalysis [5] and medicine [6].

## Progress in the Inactivation of SARS-CoV-2 Using Nanolayers Composed of Doped Metal Oxides Synthesized via Sol-Gel Processing

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This research demonstrates how nanotechnology can address health crises while also contributing to sustainable practices, specifically through the development of solutions for inactivating and eliminating SARS-CoV-2. The study focuses on the synthesis and application of metal-doped oxides, produced via the sol-gel technique, to create nanocomposites with improved photocatalytic properties. These materials, when applied as thin films and further optimized with ionizing radiation, offer a novel approach to combating the virus. This approach not only offers an innovative solution for combating SARS-CoV-2 but also highlights the role of nanotechnology in advancing sustainability in both health and environmental contexts.

**Keywords:** SARS-CoV-2, Nanocomposite, Nanotechnology

## DNA nanotechnology for personalized medicine: from selection to advances therapeutics

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Aptamers are short, single-stranded DNA or RNA sequences obtained from a random oligonucleotide library *via* systematic evolution of ligands by exponential enrichment (SELEX) technology. They can bind to a wide range of targets with high affinity and specificity, including ions, small molecules, proteins, cells, and tissues. Often referred to as “chemical antibodies”, their improved thermal and chemical stability, small size, low immunogenicity, and little to no batch-to-batch variation by chemical synthesis make them promising biorecognition tools for numerous applications including diagnosis, drug delivery, therapeutics and pharmaceutical analysis [1].

This presentation introduces the universe of aptamers, highlighting the multiple pathways they can bring specificity to the table when designing biosensors or targeted delivery systems. Our recent advancements in aptamer selection through magnetic bead SELEX technology for glycopeptide antibiotics will be presented, with possible applications in therapeutic drug monitoring and personalized treatment. Other examples include various electrochemical platform designs that combine aptamers and nanomaterials as diagnostic tools for cancer. Moreover, the use of aptamers as targeting agents on the surface of magnetic nanocarriers will be shown, for the development of novel drug delivery systems for hepatocellular carcinoma treatment [2]. The advantages and future directions for the continued development of aptamer-based personalized medicine are also discussed.

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### Acknowledgements

This work was supported by “European integration of new technologies and social-economic solutions for increasing consumer trust and engagement in seafood products (FishEuTrust)”, Grant Agreement: 101060712/2022.

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# Application of fluorescence imaging to assess in vivo the biodistribution of nanoparticles

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The use of nanoscale materials and nanotechnology in medication delivery and diagnostics is known as nanomedicine. Improved drug delivery is possible when the therapeutic is delivered to the site of action via nanoparticles. This includes specificity/targeted delivery, controlled or stimuli-responsive delivery, protection of the therapeutic from the biological milieu, penetration of biological barriers, and access to intracellular sites of action. <sup>[1]</sup> The bioavailability of nanomedicines is confronted with several obstacles, even with the advancements in nanotechnology. In order to better understand how nanoparticles, interact with living things in terms of pharmacokinetics and to ascertain how well they reach target tissues, it is crucial to evaluate their bioavailability in vivo. <sup>[2]</sup> Fluorescence imaging is one of the primary imaging techniques and approaches used in this method. To facilitate these studies, fluorescent markers are frequently applied to the nanoparticles to monitor their accumulation and dispersion within tissues. With reference to this in vivo imaging system, it is a fluorescent imaging platform intended for targeted imaging of small animals in order to monitor biodistribution, accumulation, and clearance in real time. <sup>[3][4]</sup> This enables real-time observation of the activity of nanoparticles in living things by tracking their distribution, effectiveness of targeting, release of drugs, and therapeutic results. In this presentation, we will provide an overview of application of Near-infrared (NIR) fluorescent imaging for detection of nanoparticles in live animals and excised tissue.

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# Boosting the performance of nanoporous graphene-based thin-film microelectrodes for neural interfacing

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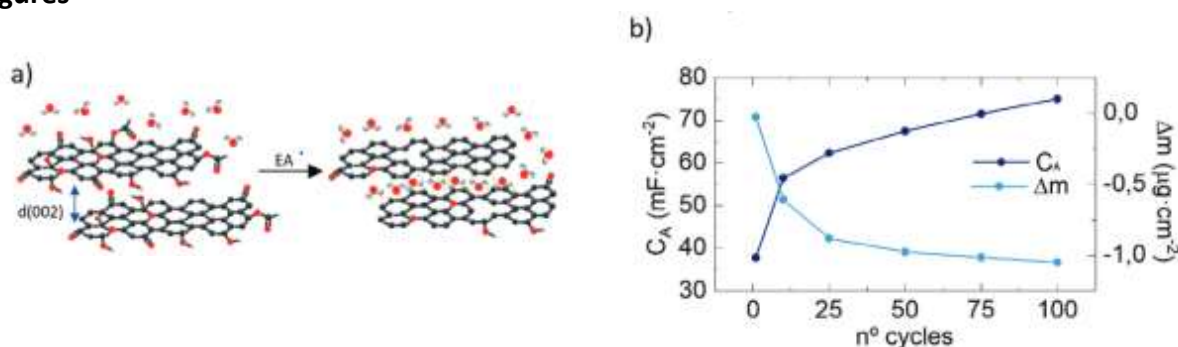
Recently, we have demonstrated the superiority of nanoporous graphene-based electrodes as neural interfaces for in vivo recording and stimulation of the central and peripheral nervous system in small animals. [1] We managed to develop a graphene thin film technology based on a large-scale fabrication of flexible microelectrode arrays. Our technology was benchmarked against standard of care revealing higher signal-to-noise ratio than platinum and better charge injection capabilities than iridium oxide. Such superior performance raises from the high capacitance and low sheet resistance of nanoporous graphene electrodes. However, achieving the optimal electrochemical performance of this technology becomes a challenge due to the difficult access of the electrolyte into the nanoconfined space of graphene. By performing a voltage-controlled electrochemical activation of nanoporous graphene electrodes we manage to exploit its electrochemical performance in terms of areal capacitance and electrochemical impedance [2]. The origin of such improvement, of utmost importance for the tailored design of high-performing electrodes based on nanoporous graphene, remains unknown. Advanced operando characterization techniques, like the presented in this work, are needed to reveal the dynamics of the irreversible material changes introduced during the graphene electrochemical activation process, including ionic diffusion and water confinement within the nanopores, along with the reduction of oxygenated groups and the decrease of the graphene interlayer distance. Furthermore, operando techniques are used to uncover the origin of the complex polarization-dependent dynamic response of graphene electrodes.

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## Figures



**Figure 1:** (a) Schematic representation of the effect of electrochemical activation on the graphene morphology. (b) Capacitance (extracted from cyclic voltammetry, CV) and mass change (from quartz crystal microbalance) as a function of the CV cycles.

# Measuring Nanoparticle Size Distribution in a Fluid Using an Interactive Force Apparatus

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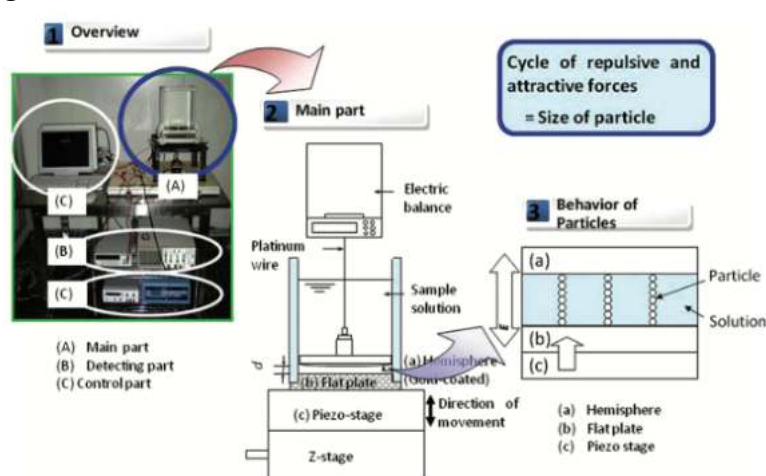
The paper explains how the Interactive Force Apparatus (IFA) can be employed to measure the particle size distribution of nanoparticles in a fluid, regardless of their concentration. The IFA technique is then compared against conventional techniques such as Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) to validate the results.

The study's results demonstrated that IFA could effectively measure the size distribution of various nanoparticles, with results consistent with those obtained via TEM and SEM. The findings suggest that IFA could significantly enhance the accuracy and applicability of particle size distribution measurements in industrial processes, particularly where high concentration and non-transparent solutions are involved. This technique can potentially improve processes related to the water purification, mineral processing, and manufacturing of new materials, where precise particle size measurement is critical.

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## Figures



**Figure 1:** Schematic diagram of the interactive force apparatus (IFA).



# Ex Situ Covalent Functionalization of Germanene via 1,3-Dipolar Cycloaddition: A Promising Approach for the Band Gap Engineering of Group 14 Xenes

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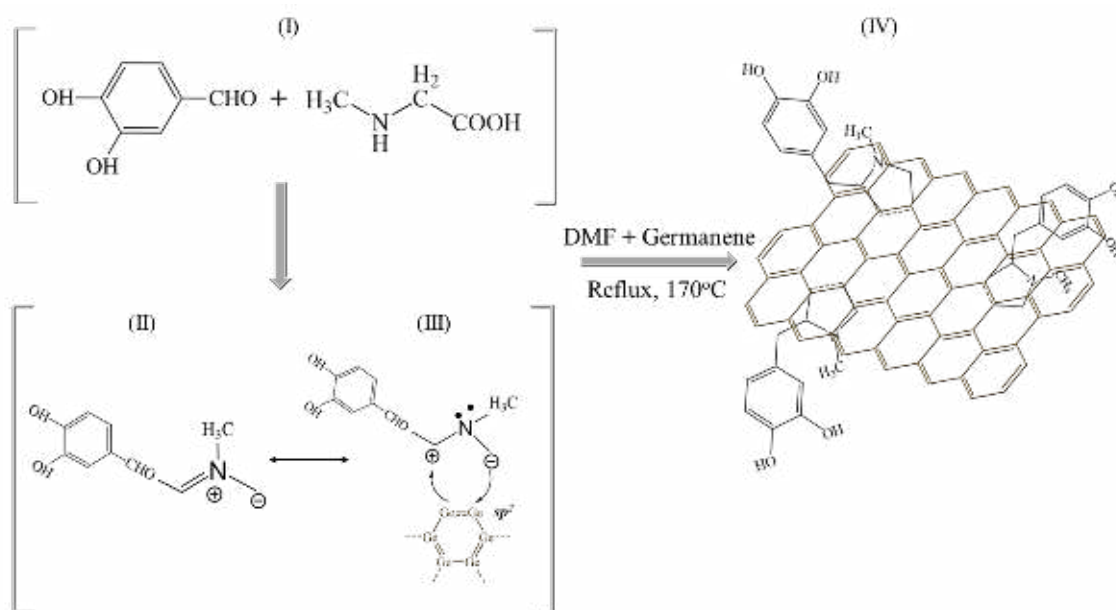
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Group-14 Xenes beyond graphene such as silicene, germanene, and stanene have recently gained a lot of attention for their peculiar electronic properties, which can be tuned by covalent functionalization. Up until now, reported methods for the top-down synthesis of covalently functionalized silicene and germanene typically yield multilayered flakes with a minimum thickness of 100 nm. Herein, we report the ex situ covalent functionalization of germanene via 1,3-dipolar cycloaddition of the azomethine ylide generated by the decarboxylative condensation of 3,4-dihydroxybenzaldehyde and sarcosine. Amorphous few-layered sheets (average thickness of ~6 nm) of dipolarophile germanene were produced by thermal dehydrogenation of its fully saturated parent precursor, germanane. Spectroscopic evidence confirmed the emergence of the dipolarophilic  $sp^2$  domains due to the dehydrogenation of germanane, and their  $sp^3$  hybridization due to the covalent functionalization of germanene. Elemental mapping of the functionalized germanene revealed flakes with a very high abundance of carbon uniformly covering the germanium backbone. The 500 meV increase of the optical band gap of germanene observed upon functionalization paves the way toward band gap engineering of other group-14 Xenes, which could potentially be a major turning point in the fields of electronics, electrocatalysis, and photocatalysis.

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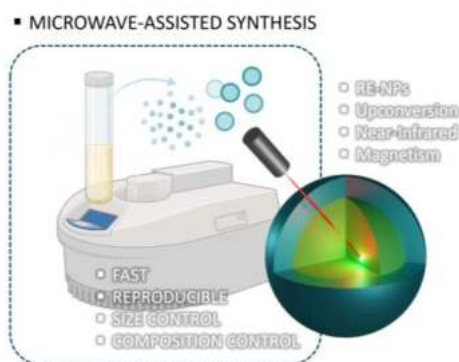
**Figure 1:** Proposed mechanism of the 1, 3 Dipolar cycloaddition reaction of azomethine ylides to the germanene layers

# Shining a Light on Lanthanide-Doped Nanoparticles: From Synthesis to Potential Applications

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The remarkable optomagnetic properties of the rare-earth elements (RE) make RE-based materials ideal for biomedical applications, including diagnostic (e.g., imaging, nanothermometry) and therapeutic (e.g., drug delivery, photodynamic therapy) approaches. This is due to the unique electronic properties of the f-elements allowing for upconversion and near-infrared emission under near-infrared excitation as well as high magnetic moments. Moreover, the temperature dependence of their optical features allows to use RE-based materials as nanothermometers for optical temperature read-out. Yet, challenges remain. Low emission intensity and efficiency of small nanoparticles (NPs), and reliable, fast synthesis routes. As material chemists, we tackle these challenges with new designs of RE-NPs by chemically controlled synthesis, application-oriented surface chemistry, and understanding of structure-property-relationships. Sodium rare-earth fluorides ( $\text{NaREF}_4$ ) are our favorite materials, and we developed a fast and reliable microwave-assisted synthesis approach allowing crystalline phase and size control in the sub 20 nm realm.<sup>[1]</sup> Such control is crucial for the understanding of fundamental structure-property relationships and to optimize their optical and magnetic properties, when aiming for the design of next-generation optical probes or contrast agents for magnetic resonance imaging. For instance,  $\text{NaGdF}_4$  NPs are gaining interest as alternative MRI contrast agents,<sup>[2]</sup> while co-doping with luminescent  $\text{RE}^{3+}$  ions renders them excellent candidates for photoluminescent optical probes. Having a fast and reliable synthesis route towards  $\text{NaREF}_4$  NPs on hand, we now explore various nanoparticle architectures and compositions with the goal to optimize their optical properties, ultimately resulting in the design of biocompatible multimodal bioprobes.<sup>[3,4]</sup> This presentation will shed light on recent results and remaining challenges in the field of RE-based nanostructures with respect to their microwave-assisted synthesis as well as structural and optical properties, seeking biomedical (and beyond) application.



**Figure 1.** Microwave-assisted synthesis of multifunctional rare-earth-based nanomaterials.

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## Spray-coated Diamond Electrode for Sulfuric Acid Electrolysis

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Boron-doped diamond (BDD) electrodes or diamond electrodes are known to be useful for a durable electrode for electrolysis with a high efficiency base on their wide potential window and physical and chemical stabilities. As a result of electrolysis of concentrated sulfuric acid at diamond electrode, reactive oxidizing species, such as peroxodisulfate, peroxomonosulfate, and hydrogen peroxide, can be generated at a high current efficiency. Such electrolyzed sulfuric acid exhibits strong oxidizing power, and is used for mineralization of organic compounds. In this study, we have developed a new method to fabricate a large-sized diamond electrode that can be used for electrolyzed sulfuric acid production by forming a BDD powder (BDDP)/silica composite film via spray coating.

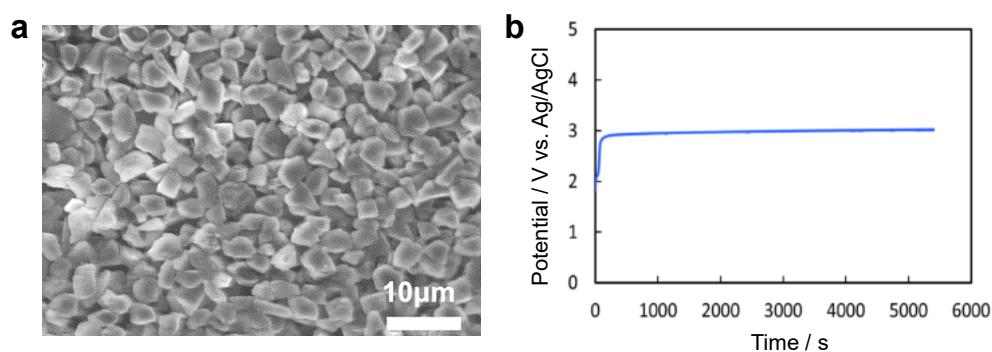
BDDP was prepared by deposition of a BDD layer on the surface of diamond powder with a particle size of 3–6  $\mu\text{m}$  via microwave plasma-assisted CVD [1]. The BDDP was added to tetraethyl orthosilicate/ethanol solution, followed by addition of ultrapure water and nitric acid and stirring to prepare a BDDP/silica sol solution. The BDDP/silica sol solution was spray-coated on a hydrophilic titanium substrate, and after baking at 150  $^{\circ}\text{C}$  for 1 h, a spray-coated diamond electrode consisted of a BDDP/silica layer formed on the substrate was obtained (Fig. 1a).

10 mL of 50% sulfuric acid was electrolyzed at a constant current density of 20  $\text{mA cm}^{-2}$  for 90 min at a spray-coated diamond electrode (electrode area: 0.5  $\text{cm}^2$ ). During the electrolysis, the electrode potential was stable around +3 V vs. Ag/AgCl, indicating that no deterioration of the electrode occurred even at highly positive potentials in concentrated sulfuric acid (Fig. 1b). Current efficiency of reactive oxidizing species formation was calculated to be 41%. These results confirm that the spray-coated diamond electrode can be used for electrolyzed sulfuric acid production. A large-sized spray-coated diamond electrode was also prepared in the same way using a 20 $\times$ 20  $\text{cm}^2$ -sized titanium substrate. Therefore, the spray coating method is expected to be useful for scaling up of a diamond electrode for sulfuric acid electrolysis.

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### Figures



**Figure 1:** (a) SEM image of spray-coated diamond electrode surface. (b) Electrode potential during electrolysis (20  $\text{mA cm}^{-2}$ ) of 50%  $\text{H}_2\text{SO}_4$  at spray-coated diamond electrode.

# Beyond Nanoparticles: Advanced Microencapsulation Techniques in Paediatric Pharmaceutical Formulations – A Comprehensive Analysis of the Prilling/Vibration Method and Case Studies

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## Abstract

Microparticles offer a practical and well-established alternative for paediatric drug delivery, particularly when compared to nanoparticle systems. Their larger size inherently reduces the risk of systemic absorption, which minimizes side effects and makes them safer for children.[1] Additionally, microparticles are highly versatile and can be engineered for a range of applications, such as taste masking, colonic delivery, and precise dosage regulation (Figure 1). For instance, they can effectively mask unpleasant medication flavors, which is crucial for improving adherence among young patients. Moreover, microparticles can be tailored to release drugs like anti-inflammatory corticosteroids and probiotics specifically in the colon, enhancing the treatment of gastrointestinal disorders.[2] One of the key advantages of microparticles in paediatric care is their ability to regulate dosage, especially when only adult formulations are available. By engineering microparticles to deliver lower, child-appropriate doses, it is possible to ensure both safety and efficacy in paediatric treatments. This capability is particularly important when adapting adult-formulated drugs for children, allowing for customized treatment that meets the unique needs of paediatric patients without compromising therapeutic outcomes. [3] Among the various techniques for producing microparticles, the prilling/vibration method stands out for its ability to precisely control particle size and morphology. [2] This control is crucial for achieving consistent drug release and optimizing therapeutic outcomes in paediatric applications. Case studies recently published by our group have demonstrated the effectiveness of this method in above cited areas. [3-6] The method's ability to create uniform microparticles with tailored properties further underscores its value in developing paediatric formulations. In summary, while nanoparticle-based systems have potential, microparticles, particularly those produced via the prilling/vibration method, offer a more reliable and immediately applicable solution for paediatric drug delivery. The proven advantages of microparticles is essential for developing safe, effective, and practical therapeutic options for children.



**Figure 1:** Microparticles produced by the prilling/vibration method meet various needs in paediatric patients.

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Noble metal nanoparticles possess remarkable attributes that make them ideal scaffolds for the development of highly sensitive sensing devices. Their inherently high surface-to-volume ratio, coupled with their unique optical and electrical properties, renders them extremely responsive to changes in their surrounding environment.[1] One of the key advantages of noble metal nanoparticles lies in their tunability through molecular functionalization. By modifying their surface chemistry with tailored molecular receptors, their properties can be finely adjusted to suit specific sensing applications. In my lecture, I will present our recent findings on the functionalization of gold nanoparticles (AuNPs) to engineer hybrid systems suitable for various sensing applications.

I will present a work focused on developing chemiresistors (CRs) using three dimensional (3D) networks of AuNPs bridged by supramolecular receptors (dithiomethylene dibenzo-18-crown-6 ether, DTDB-18C6) for potassium ions (K<sup>+</sup>) sensing. These CRs demonstrate linear sensitivity, high selectivity, stability, reversibility, fast response time, and compatibility with microfluidic systems, making them promising for point-of-care (POC) sensing, particularly in health monitoring.[2]

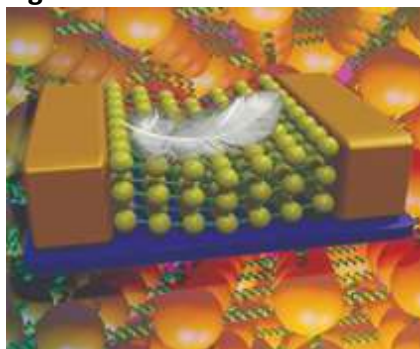
Furthermore, I will introduce a novel strain sensor employing AuNPs interconnected by flexible molecular linkers. This strain sensor, when deposited onto flexible supports, demonstrates exceptional sensitivity to both compressive and tensile strain. Its remarkable properties, including high flexibility, rapid response time, and robustness, enable high-resolution monitoring of artery pulse waves for accurate health assessment.[3]

Looking forward, continued exploration of noble metal nanoparticle functionalization holds promise for further advancements in sensing technologies, potentially revolutionizing healthcare and wearable monitoring devices. Additionally, leveraging these hybrid systems in other sensing applications could lead to breakthroughs in various fields, including environmental monitoring and industrial process control.

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### Figures



**Figure 1:** Strain sensor based on AuNPs interconnected by flexible molecular linkers.



# Soft Layered Conjugated Polymers for Advanced Sensing

Yuya Oaki

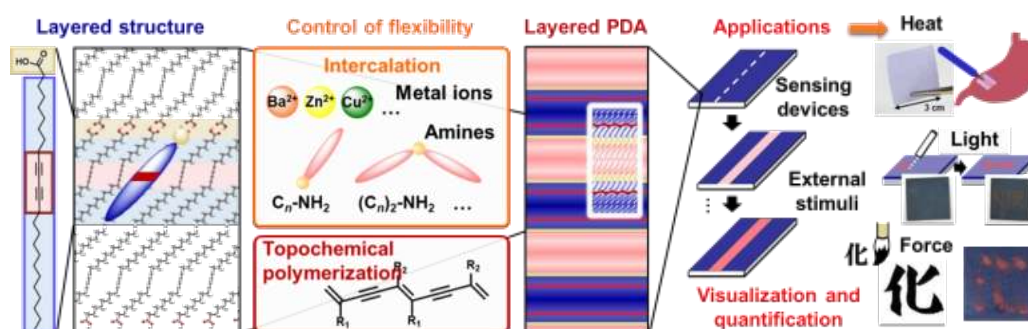
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Two-dimensional (2D) nanostructures have attracted much interest in recent years. Our group has focused on structures and functions of soft layered materials.<sup>[1]</sup> Compared with the conventional rigid layered compounds, soft layered materials have potentials for the molecular motions exhibiting dynamic functions. For example, the soft layered composites are efficiently exfoliated into the nanosheets.<sup>[2]</sup> The designed organic layered materials are synthesized and applied to energy-related devices.<sup>[3,4]</sup> Here I focus on a soft layered material based on conjugated polymers, layered polydiacetylene (PDA), exhibiting the structure flexibility and dynamic properties (Figure 1).<sup>[1,5-15]</sup> PDA shows blue-to-red color changes with the application of external stimuli through shortening the effective conjugation length with the motion of the layered structures. The dynamic color-change properties, *i.e.* the responsivity, are controlled by the intercalated guests. The responsivity control is achieved by the integration of stimuli-responsive materials. A variety of external stimuli, such as heat,<sup>[5-9]</sup> light,<sup>[10]</sup> and force,<sup>[11-15]</sup> are visualized and quantified using the soft layered conjugated polymers. The sensors can be applied in the field of clinical medicine.<sup>[9,12,15]</sup>

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**Figure 1:** Schematic illustrations of layered polydiacetylenes (PDAs) and their advanced sensing applications.



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## Abstract

Epidermal bioelectronic devices show great promise in healthcare due to their ability to provide longitudinal monitoring as well as on-demand delivery to maintain optimal health status and evaluate patients' physical conditions. Epidermal biosensors are at the center of this effort and offer a vast potential to revolutionize conventional diagnostics that uses traditional laboratory tests-based evaluations, usually called 'clinical labs,' that are slow and mainly require in-person visits and frequent invasive sampling if the long-term analysis is necessary. In this presentation, I will give a brief overview of our recently developed epidermal diagnostic approaches targeting various metabolites, hormones and microorganisms as well as some of skin physical and chemicals parameters to acquire better knowledge on early diagnosis and disease progression particularly for metabolic diseases and infections. This talk will summarize how to design epidermal sensors, integrated electronics and how to use them in clinical setting with our unique access to patient materials, which creates an unprecedented opportunity to address fundamental questions in medical diagnostics.[1]

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# Biomolecular changes in cervical cancer cells by non-stabilised and albumin-stabilised colloidal N-TiO<sub>2</sub> nanoparticles: SR FTIR spectroscopical approach

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The presented research focuses on the intracellular changes induced by N-doped TiO<sub>2</sub> (N-TiO<sub>2</sub>) nanoparticles (NPs) in cancer therapy, using cervical cancer as a model system. Uncovering the underlying intracellular mechanisms and the interplay between various signalling pathways that lead to cell death and the elimination of cancer cells is essential. A general approach to beat cancer and minimise severe side effects is to apply controlled and targeted therapy. Among other techniques, photodynamic therapy is promising, as it uses light to externally activate a drug with photosensing properties and control tumour elimination. To increase efficiency, applying NPs as drug carriers or as photosensitisers (PSs) is advantageous [1]. TiO<sub>2</sub> NPs are promising as carriers and PSs due to their good photo-catalytic properties. On the other hand, due to its wide gap, only photoactivation with UV light is possible. Doping of TiO<sub>2</sub> with different elements, such as nitrogen [2] can change its bandgap, allowing its activation with visible light.

Our approach to assessing biomolecular changes is through applying Synchrotron Radiation Fourier Transform Infrared Spectroscopy (SR FTIR). This method, known for its high photon flux, allows us to understand intracellular biomolecular changes in cervical cancer cells (HeLa) caused by pristine N-TiO<sub>2</sub> and N-TiO<sub>2</sub> stabilised by bovine serum albumin (BSA-N-TiO<sub>2</sub>). The high spatial resolution and precision of SR FTIR increase the accuracy of the research. It can be performed on whole cells and tissues immobilised on a CaF<sub>2</sub> carrier, providing a detailed assessment of biomolecular intracellular changes both qualitatively and quantitatively in different regions of cells. These involve changes in lipids, nucleic acids and proteins. Our results demonstrate that stabilising N-TiO<sub>2</sub> with BSA induces different structural changes in the proteins compared to pristine N-TiO<sub>2</sub>. These changes are more expressed in the vibrational region of  $\beta$ -sheets, whereas both NPs cause changes in the area of  $\alpha$ -helices. In addition, significant changes in the nucleic acid region were also detected in treated cells compared to the control. In summary, by using SR FTIR, we have demonstrated significant biomolecular changes in cells treated with N-TiO<sub>2</sub> and BSA-N-TiO<sub>2</sub>, implying that the stabilisation of NPs with serum albumins plays a role in controlling the NPs' cellular action.

**Acknowledgements:** This work was supported by Serbian Ministry of Sciences, Technological Development and Innovation (Grant No. 451-03-47/2024-01/200017), Spanish Ministry of Science and Innovation (MCIN/AEI/10.13039/501100011033) through project PID2021-122613OB-I00, Serbia-Germany bilateral cooperation programme (337-00-253/2023-05/3). SR-FTIR experiments were performed at the MIRAS beamline at ALBA Synchrotron with the collaboration of ALBA staff (experiment No. 2023027513).

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## Abstract

The solution-based processing of mixed halide perovskite (HP) devices at relatively low temperatures offers prospects of developing low-cost multifunctional devices developed at flexible substrates. Hereby, we present results on using HP for demonstrating efficient solar cells and optoelectronic synapses based on the same material stack.[1-2] These devices, however, exhibit variability in their switching characteristics, weak endurance, and retention, which limit their performance and practical use. To address this challenge, we applied low-dimensional perovskite capping layers onto 3Dmixed halide perovskites using two perfluoroarene organic cations, namely (perfluorobenzyl) ammonium and (perfluoro-1,4-phenylene)dimethylammonium iodide, forming Ruddlesden–Popper and Dion–Jacobson 2D perovskite phases, respectively.[3] The corresponding mixed-dimensional perovskite heterostructures were used to fabricate resistive switching memories based on perovskite solar cell architectures, showing that the devices based on perfluoroarene heterostructures exhibited enhanced performance and stability in inert and ambient air atmosphere. Notably, the substrate on which the perovskite active layer is developed has been reported to severely affect its quality and thus the overall device performance. Hereby, we demonstrate the sustainable manufacturing of memristive perovskite solar cells by replacing the expensive poly[bis(4- phenyl)(2,4,6-trimethylphenyl)amine] (PTAA) that serves as a hole transporting layer (HTL) with a self-assembled monolayer (SAM), namely [2-(3,6-dimethoxy-9H-carbazol-9-yl)ethyl]- phosphonic acid (MeO-2PACz).[4] Multiple sequential memristive current–voltage characteristics of single devices are reported, and average data of multiple reference and targeted devices are compared. Resistive switching memory devices based on SAM exhibit improved performance having reduced average SET voltage values and narrower statistical variation compared to reference devices with PTAA. It is shown that both PTAA and SAM based devices exhibit high ON/OFF ratio of about  $10^3$  operating at low switching electric fields. Replacing an expensive polymer-based HTL with this approach reduces fabrication costs compared to PTAA. Recent results on lead-free double perovskite based resistive memory devices will be presented toward achieving enhanced sustainability.

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## Acknowledgments

The work has been supported by the National Foundation for Research and Innovation of Greece under project INTELLECT (no. 81045).

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Hydrogen has potential to develop a cleaner and more sustainable world. It is used as transportation fuels, chemicals in industry, or heating source. There are several techniques to produce hydrogen such as water electrolysis, steam reforming, or biomass from trees or agricultural crops[1]. Of these methods, water electrolysis has some advantages. It can be conducted at moderate conditions and the reactions can be easily controlled by adjusting the applied potential or current. However, in the conventional water electrolysis system, both hydrogen and oxygen generate at the same time, and this causes some problems[2]. High operating pressures and the pressure difference between hydrogen and oxygen require high durable separators. There is also safety issue caused from gas mixing because of the co-generation of hydrogen and oxygen at the same time and place. If water electrolysis is decoupled, and hydrogen and oxygen evolution are separated, these kinds of problems will be solved. An operational flexibility will be improved as well. Our aim of this work is to produce hydrogen and oxygen separately by using redox species as a mediator. In this work, iodide and iodate ion couples were used to investigate the decoupled water electrolysis which proceeds in two reaction steps. To find in which potential the redox reaction happens and in which potential hydrogen or oxygen starts to generate, relationships between applied potential and current were measured. At the determined potential by forementioned technique, electrolysis was conducted by using a two-compartment cell. At the first reaction step, only hydrogen generated and at the other side of the cell conversions from iodide ions to iodate ions proceeded with the maximum Faraday efficiency of 98%. At the second reaction step, only oxygen generated from one side and conversions from iodate ions to iodide ions proceeded with the maximum Faraday efficiency of 100% at the other side. Therefore, both hydrogen and oxygen were separately and efficiently produced by using iodine redox species.

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Figure

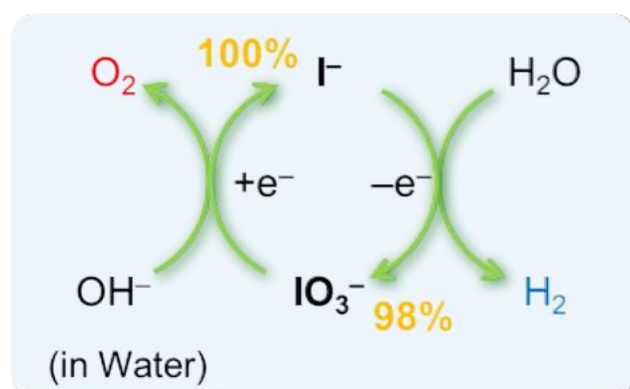


Figure 1: Outline of decoupled water electrolysis system using iodine redox species.

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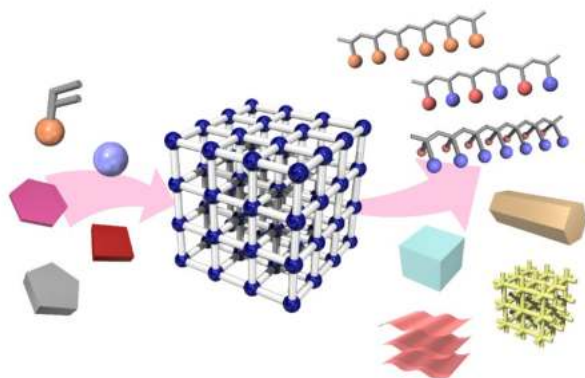
Metal-Organic Frameworks (MOFs) composed of metal ions and organic ligands have been extensively studied. The characteristic features of MOFs are highly regular channel structures with controllable pore sizes approximating molecular dimensions and designable surface functionality. Thus, MOFs have been successfully applied in numerous domains, including storage and separation, catalysis, energy, and sensing. However, the majority of relative studies in the early stages of MOF research focused on gas and solvent molecules as guests, despite the potential of infinite nanochannel structures for the encapsulation of macromolecules.

Since 2005, we have utilized the regular and tunable channels of MOFs for a field of polymerization, which can allow multi-level controls of polymers, nanoparticles, and nanographenes (Figure 1).<sup>[1]</sup> In addition, construction of nanocomposites between MOFs and polymers provides unprecedented material platforms to accomplish many nanoscale function.<sup>[2]</sup> We have also developed direct insertion of polymers into nanochannels of MOFs, which enables powerful macromolecular recognition and separation technologies with exceptionally high selectivity.<sup>[3]</sup> Designing nano-sized pores of MOFs with a regular arrangement of reactive/interactive/responsive entities offers the possibility of universal polymer production and purification that cannot be accomplished by conventional methods.

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### Figures



**Figure 1:** Controlled polymerizations using MOFs

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Oral delivery of nucleic acid therapies offers new therapeutic possibilities for management of local and systemic disease and enables rapid mass immunisation. However, presently there are no systems for oral delivery of nucleic acids. Synthetic systems suffer from poor stability in the gut and poor delivery efficiency. Extracellular vesicles (EVs) from bovine milk are highly capable of crossing the intestinal epithelium.<sup>1</sup> These are potentially interesting systems from a widely available source and there is clear evidence that milk EVs resist digestion and are absorbed systemically intact. Milk EVs therefore have significant potential as safe and inexpensive delivery systems. However, loading of EVs with macromolecules is currently a significant challenge as current drug loading methods are either inefficient or destructive (or both). We investigated the stability of milk EVs in intestinal fluids and their ability to permeate the intestinal epithelium, including in tissue-derived human intestinal organoids. We further loaded milk EVs with siRNA (as a model therapeutic) using different methods and show successful, functional delivery of this payload in cells and an animal model of inflammatory bowel disease (IBD).

Milk EVs were isolated using ultracentrifugation and characterised for expression of common exosomal proteins, as well as size (nanoparticle tracking analysis, dynamic light scattering), charge (zeta potential) and morphology (electron microscopy). Milk EVs were tested in fed-state and fasted-state simulated intestinal fluids using a fluorescent membrane probe. Epithelial permeability was tested in Caco-2 monolayers and human tissue biopsy-derived intestinal organoids, cultured as monolayers or with 'apical-out' polarity. EVs were loaded with siRNA through electroporation or by fusion with cargo loaded lipid nanoparticles. siRNA-loaded EVs were tested for downregulation of target proteins (GAPDH) or inflammatory response in cells and in a rat model of IBD.

Milk EVs showed superior stability in simulated intestinal fluids compared to liposomes and efficiently permeated Caco-2 monolayers. EVs clearly transported across 3D 'apical-out' and monolayer human intestinal epithelial organoids. Milk EVs loaded with siRNA induced gene silencing and anti-inflammatory siRNA-loaded EVs reduced inflammation in an IBD rat model.<sup>2</sup>

Overall, the work shows that milk EVs could act as natural and safe systems for oral delivery of nucleic acid therapies.

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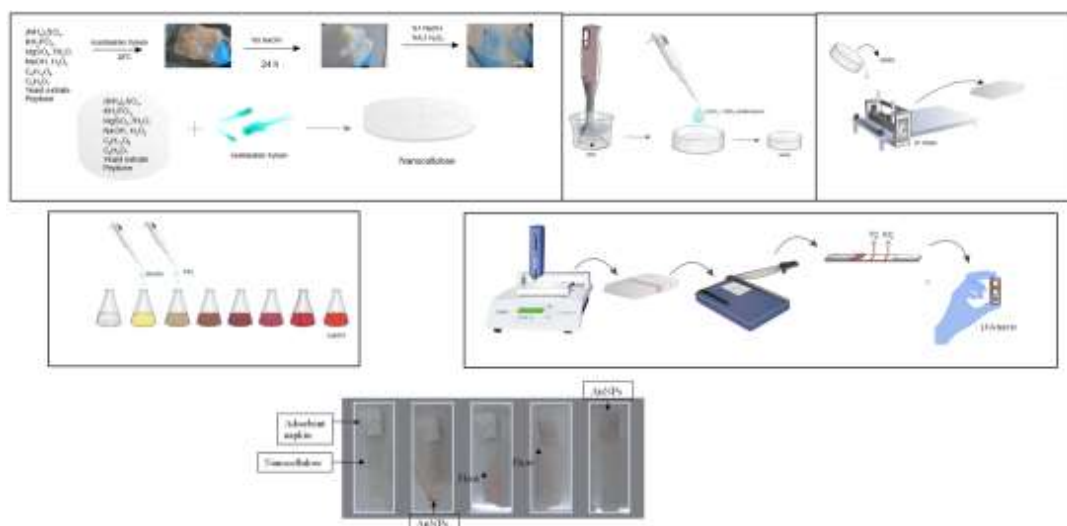
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Lateral flow biosensors are paper-based devices that allow the detection of different types of analytes with quickness, robustness and selectivity, without leaving behind paper sensors benefits as low-cost, recyclability and sustainability [1]. LFA consists of four basic components: sample pad, conjugation pad, detection pad (nitrocellulose membrane) and waste pad. The nitrocellulose membrane is an important component of the LFA system where signals are generated. The performance of the nitrocellulose membrane directly affects the accuracy and reproducibility of a test result. However, the sensitivity of this type of biosensors is not always as high as required, often not permitting a clear quantification [2]. With the recent advances in nanomaterials, great effort has been devoted to the development of miniaturized analytical platforms [3]. Taking advantage of the nanocellulose, in this talk, the use of bacterial nanocellulose (BNC) as a nanobiomaterial obtained from *Acetobacter xylinum* culture, exhibiting distinctive properties such as biocompatibility, optical transparency, hydrophilicity, high porosity, and high surface area with hydroxyl-containing groups and high mechanical strength will be overviewed.

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### Figures



**Figure 1:** The production process of bacterial nanocellulose-based LFA

**Acknowledgements:** This study is supported by the Scientific and Technological Research Council of Türkiye (TÜBİTAK), Grant number: 123Z712.

# MoS<sub>2</sub>-PEDOT:PSS Nanocomposite-Based Electrochemical Sensor for Epirubicin Detection in Biological Samples

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Cancer is a group of deadly diseases that can begin in almost any part of the body, where cells grow uncontrollably and spread to other areas [1]. Among cancer treatment methods, chemotherapy, which uses antineoplastic agents, is considered the most effective approach. However, it is well known that chemotherapy affects both cancerous and healthy cells due to the high doses of drugs intake, which results in significant side effects throughout the body [2]. As a result, tracking the dosage of anticancer drugs in biological fluids like human blood or urine is crucial for evaluating potential side effects and the overall effectiveness of the chemotherapy treatment. Epirubicin (EPB), a widely known antineoplastic drug from the anthracycline antibiotics group, is commonly used to treat certain types of cancer, including breast and lung cancer [3]. Chemically exfoliated molybdenum disulfide (CE-MoS<sub>2</sub>) nanosheets were successfully synthesized through a metal intercalation method and subsequently modified their surfaces with Poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS), a conductive polymer. The structural, morphological, and electrochemical characterizations of the CE-MoS<sub>2</sub>/PEDOT:PSS nanocomposite were conducted using X-ray photoelectron spectroscopy (XPS), thermogravimetric analysis (TGA), transmission electron microscopy (TEM), and electrochemical impedance spectroscopy (EIS). A portable electrochemical sensing platform was developed by modifying a screen-printed carbon electrode (SPCE) with the CE-MoS<sub>2</sub>/PEDOT:PSS nanocomposite. The electrochemical behaviour of EPB was investigated on the SPCE modified with the CE-MoS<sub>2</sub>/PEDOT:PSS nanocomposite using cyclic and differential pulse voltammetry. The CE-MoS<sub>2</sub>/PEDOT:PSS/SPCE exhibited promising electrocatalytic activity for the oxidation of EPB, showing an analytical performance in the concentration range of 0.06 to 9.30 µM, with a low detection limit of 44.3 nM. Additionally, it was successfully analysed human plasma samples containing EPB using the CE-MoS<sub>2</sub>/PEDOT:PSS/SPCE, achieving satisfactory recovery rates.

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## Abstract

This work investigates the diffusion and permeation of helium in various plastic bottles through a nanoscience lens, using both Steady State and Time Lag methods. Helium, with its small atomic size, serves as an ideal probe for studying gas transport at the nanoscale within polymers. The nano-structured characteristics of polymers, such as chain density, free volume, and molecular interactions, significantly influence gas diffusion and permeation behaviours. By applying the Steady State method for equilibrium transport and the Time Lag method for transient behaviour, we extract key diffusion and permeation coefficients that reveal how nano-structural features of the polymer affect gas transport. These findings contribute to a deeper understanding of how nanoscale properties of materials govern macroscopic behaviours, which has implications for industries like packaging, pharmaceuticals, and materials design, where precise control of gas barriers is critical. Our study underscores the importance of integrating nanoscience concepts into the analysis of gas diffusion, demonstrating the potential for enhanced material performance through targeted nano-engineering.

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# Exploring Aryl Radicals as Multifunctional Agents for (Nano)material Surface Modification: A Comprehensive Review with a Focus on DFT Analysis

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Aryl radicals derived from aryldiazonium cations have emerged as a leading choice for surface modification since their innovative introduction by Professor Pinson in the 1990s [1]. Unlike traditional surface modification agents such as thiols, silanes, and phosphonic acids, aryldiazonium cations offer a more versatile and straightforward method for surface functionalization. This technique proves effective across a broad spectrum of materials [1-4], regardless of their chemical composition or electrical conductivity. In contrast, other agents have limitations: thiols primarily work with noble metals and are ineffective with polymers, while phosphonic acids and silanes are usually limited to surfaces with oxy-hydroxy groups [5].

Herein, we explore the atomistic modelling of diazonium salt grafting mechanisms, energetics, and stability on various substrates, including metals, carbon-based materials, silicones, and phosphorus-based compounds [3]. It examines crucial aspects such as dissociation, the grafting process, and the spectroscopic signatures of diazonium salts. Furthermore, density functional theory (DFT) calculations provide insights into the stability of the formed interfaces, which is challenging to measure directly in experiments that typically capture only the average (collective properties) stability of the layer (e.g., through thermogravimetric analysis). DFT spectroscopic analysis reveals distinctive characteristics of aryl grafting, and when combined with experimental results from vibrational spectroscopies, it allows for the first-time assignment of the Au-C(alkyl) bond [3,6].

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### Abstract

Prostate cancer is the most common form of non-skin cancer affecting men between the ages 45 to 60 years old. Diagnosed as the 4<sup>th</sup> most common cancer worldwide, this disease affects millions of men around the world, especially patients from developed regions. It has a low mortality rate and an ever-increasing rate of being cured if caught in the early to mid-range phases of the disease. This type of cancer is characterised by an aberrant and uncontrolled growth of abnormal cells in the prostate gland, which can be detected by blood tests, MRI, digital screening and prostate biopsy. One of the leading factors which has been disputed as causative of prostate cancer is the genetic aspect. These alterations include, but are not limited to mutations affecting the PTEN and Tp53 gene, fusion of the TMPRSS2 gene with the ETS genes, HOXB gene and lately as a novel indicator of prostate cancer, the KLK15 gene. Human kallikreins (KLK) proteins serve for a variety of functions in the human body ranging from immune responses, formation of the teeth enamel, peeling of skin and liquefying the semen. Higher expression of this gene could lead to the occurrence of pathological conditions of the aforementioned functions. Being a novel predictor gene, our focus was to elucidate the point mutations affecting this gene and their potential damage resulting in cancer. Twenty-five-point mutations were analysed via in silico methods to understand and elucidate the role these mutations have in the KLK15 gene in the prostate. To assess the role of these mutations and their possibility of being involved in the disease, 4 predicting algorithms were used (SIFT, PolyPhen-2, FATHMM and SNPs&GO). To predict the secondary structure, surface accessibility and protein stability we used NetSurfP3.0 and I-Mutant 2.0. Four mutations were found to be damaging to the KLK15 gene, I164M, D231Y, C242F and Y244S, with high deleterious effect causing significant structural and functional changes in the protein. These predictions help identify novel and potential point mutations, their uncharacterised function in the gene and possibility to be targeted by pharmaceutical drugs to counteract the effects of prostate cancer.

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The immunosystem plays a crucial role in tumor development and progression. Macrophages associated to the tumor can reach the half mass of solid tumors and play a dual function based on their phenotype and can differentiate into tumor suppressor M1 or pro-oncogenic M2 phenotype. In this context, recently M1-macrophage derived extracellular-vesicles (M1-EVs) attracted the attention of researches thanks to their capability to reach the tumor tissues and deliver bio-derived payloads which induce the in-situ shift of macrophages from M2 to M1, thus providing an anti-cancer effect [1]. To maximize the effectiveness of this nanosystem, the aim of this work is to combine thermoresponsive synthetic liposomes and M1-EVs to realize a hybrid bio-inspired nanovesicles capable of target tumor tissues and release the payloads under the application of external hyperthermia. EVs were isolated from both M0 and M1 murine macrophages and were physicochemically characterized in terms of size distribution, diameter and surface features. After that the hybridization process with thermoresponsive liposomes were carried out by freeze-thaw technique and was validated by FACS analysis. The thermoresponsiveness of resulting hybrid nanovesicles was investigated by using a fluorescent probe through the study of its release at 37°C and 42 °C. Obtained results confirmed a massive and significant higher release during the first 1 h of incubation at 42°C than 37°C. Targeting properties of engineering nanovesicles were in vivo demonstrated in murine melanoma model, showing a higher accumulation of hybrid thermoresponsive M1-EVs/liposomes than conventional liposomes. These results strongly empathize the potential use of engineering bioinspired nanosystem the development of a targeted and stimuli-responsive personalized melanoma therapy.

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Anaemia is a blood disorder that affects individuals of all ages, genders, and ethnicities. It results from a deficiency in the number or quality of erythrocytes; or haemoglobin concentration in blood, leading to a deficit in oxygen transport. Anaemia is often a symptom of other diseases, which can make its diagnosis difficult [1]. Anaemia can be classified into different phenotypic groups, such as: haemolytic, normocytic, microcytic, macrocytic, hypochromic, and Iron Deficiency Anaemia (IDA), among others [2,3]. These have different causes and treatments and its diagnosis typically involves the measurement of several key biomarkers in patients' blood, such as haemoglobin (Hb) concentration, erythrocytes' physical parameters, serum iron and serum ferritin levels. Current methods for anaemia diagnosis rely on blood analysis and a complete haemogram. Herein, we developed a nanobiosensor for the electrochemical detection of Hb based on the interaction between methylene blue (MB) and Hb on screen printed carbon electrodes (SPCE). This detection method could be used for developing a Point-of-Care (PoC) biosensor, which will be user-friendly, fast, and less invasive, requiring only a small drop of blood. Additionally, it could serve as a screening and monitoring tool for other disease states in which anaemia is a symptom.

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**ACKNOWLEDGEMENTS:** ICN2 is funded by CERCA programme, Generalitat de Catalunya. Grant SEV-2017-0706 funded by MCIN/AEI/ 10.13039/501100011033. This project has received funding from NanoAnaemia, Grant PLEC2021-007727 funded by MCIN/AEI/ 10.13039/501100011033 and by the "European Union NextGenerationEU/PRTR".

# Electrochemical miRNA Detection using Gold-Decorated Reduced Graphene Oxide Modified Paper Electrodes

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## Abstract

Paper-based biosensors are recognized as simple, cost-effective platforms for analytical testing and diagnostics. Over the last decade, they have gained significant attention due to their ease of use, disposability, and low-cost production [1]. These sensors also offer advantages like rapid analysis and the ability to work with small sample volumes, making them promising alternatives to conventional point-of-care devices [2]. Electrochemical detection techniques are cost-effective and offer high selectivity and sensitivity. Paper-based sensors can be perfectly integrated with electrochemical techniques. A standard paper-based electrochemical sensor typically consists of a paper substrate, an electrode area, and two or three electrodes [3]. Cancer, one of the most common genetic diseases, is associated with miRNAs due to their crucial role in regulating gene expression. miRNAs function as either oncogenes or tumor suppressors by inhibiting their respective oncogenic or tumor-suppressive target mRNAs [4]. For instance, miRNA-15, miRNA-16, miRNA-21, miRNA-155, and miRNA-372 are found to be significantly overexpressed in various tumors, contributing to oncogenesis [5]. In this study [6], a paper-based electrochemical biosensor was developed for the rapid and sensitive detection of miRNA-21, aiding in the early diagnosis of lung cancer. The working electrode area was modified with a hybrid structure of reduced graphene oxide and gold nanoparticles. The entire process of our assay, from electrode modification to miRNA detection, was completed in just 35 minutes, with a detection limit 12 nM for miRNA-21 target sequence [6]. Moreover, our biosensor demonstrated sufficient selectivity to differentiate the target miRNA from single-base mismatch miRNA or non-complementary miRNA sequences.

## Acknowledgements

Arzum Erdem Gürsan and Pagona Papakonstantinou acknowledge the financial support as the PI of the joint project supported by Turkish Scientific and Technological Research Council (TUBITAK; Project no. 215Z702) and British Council (Newton fund, Institutional Links, Ref: 216182787). Arzum Erdem Gürsan would like to express her gratitude to the Turkish Academy of Sciences (TUBA) as a Principal member for its partial support.

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To date, the main challenge for controlling plant bacterial diseases is to find effective ecofriendly and practical antibacterial molecules able to contrast their spread in nature. Although banned in EU countries, the use of antibiotics against bacterial infections is dramatically ongoing in non-EU countries, causing serious antibiotic resistance challenges. In the last decade, the use of nano-biomolecules, such as the bacteriophages (bacteria killer), the antimicrobial peptides (AMPs), and Aptamers (Apta), has attracted interest as promising approaches to cope with plant diseases infections and control, due to their high antipathogenic activity, low toxicity to the host plant and environment and the slower emergence of resistance. In this context, the efficiencies of these three types of nano-biomolecules were explored through the identification, characterization, and application on challenging phytopathogenic bacteria, i.e., *Erwinia amylovora* (Ea), *Xylella fastidiosa* (Xf), and *Xanthomonas campestris* pv. *campestris* (Xcc); notorious for their high threats to global agriculture, causing severe diseases in hundreds of plants and fruit tree species.

In our study, two new bacteriophages species, named “*Erwinia amylovora* bacteriophage EP-IT22” and “*Xylella fastidiosa* bacteriophage MATE 2”, belonging to the family *Myoviridae* and the genus *Carpasnavirus* were identified, respectively [1, 2]. EP-IT22 showed a circular genome of 174,346 bp containing 310 open reading frames (ORFs), whereas MATE 2 showed to have a linear genome with 63,695 bp (95 ORFs), and lacked lysogenic, virulence, antibiotic resistance, and toxin genes. *In-vivo* assays, EP-IT22 prevented fire blight symptoms in pear plants 40 days post-inoculation [2]; whereas MATE 2 showed *In-vitro* antibacterial activity on *Xf* cells.

At the AMPs level, the *Lactococcus lactis* subsp. *lactis* strain ATCC 11454 (*L. lactis*), known for its production of nisin A, and a cocktail of AMPs were used as control strategies for *Ea* and *Xf*. The results showed that 4 AMPs, out of 8 tested, and nisin A were involved in a strong antagonistic activity against both bacteria [3, 4]. The minimal lethal concentration of the AMPs and nisin A were *ca.* 0.6 mg/mL. *In-planta* tests, the AMPs and nisin A demonstrated the ability to tackle *Ea* and *Xf* infections within *Nicotiana benthamiana* plants that remained asymptomatic 74 days post inoculation.

The attempt to develop *Xf*-specific aptamers was conducted through the Cell-SELEX method, comprising 10 rounds of exposure to *Xf* and 4 rounds of counter-selection to a similar bacterium (*Xcc*), to increase the ligand specificity of the aptamers for *Xf*. Analyses of sequence libraries obtained by Cell-SELEX identified 2 highly competent aptamers on which to develop innovative laboratory diagnostic assays for *Xf*. The efficiency of nano-biomolecules in the diagnostics and control of phytopathogens is steadily increasing, making them perfect for smarter, innovative, and environmentally friendly use in agriculture.

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## Next Generation Sequencing: Applications of Oxford Nanopore Technologies to Juvenile Aphrophoridae Niche

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Blind DNA extraction from biological samples, including plants and animal tissue, microorganisms, and non-biological matrices, is a must-use for unconventional approaches or first approach to complex phenomena. In this context, Oxford Nanopore Technologies provides a comprehensive range of DNA library tools, giving streamlined access to long-read and real-time sequencing benefits. The library construction protocol covers over 86 procedures for step-by-step experimental guidance, and the specific recommendations for library preparation are based on sample type, input quantity, and experimental priorities.

In particular, MinION longer reads advantage the genome analysis, offering easier assembly, and higher accuracy in identifying and distinguishing repeating sequences. The raw genomic data produced by the device offer excellent chances for finding species but require significant downstream processing and analysis.

Our study was focused on the niche of juvenile spittlebugs: a self-produced liquid froth embedding the aquatic insects into minuscule habitats. The Meadow Spittlebug, *Philaenus spumarius*, has recently become famous for its primary role in the *Xylella fastidiosa* subsp. *pauca* ST53 transmission, the pathogen causing OQDS in Southern Italy. The Meadow Spittlebug is still the key pest of the Mediterranean olive orchard. We plated the froth (or foam) on a nutrient agar medium (Thermo Fisher Scientific, Waltham, MA, USA) by soaking sterile stabs and isolated four different bacteria entities based on color. We adopted a DNA extraction method with CTAB modified [1] to further accelerate the sample preparation process. Libraries were obtained by the Rapid Barcoding Sequencing protocol, with some modifications (magnetic particles, Mag-Bind Total Pure NGS, Omega Biotek), sequenced by means of the MinION device, and the output data analysed by means of *ad hoc* bioinformatic tools from the sequences quality checking and cleaning to their taxonomic profiling. The sequences obtained determined the presence of the genera *Microbacterium*, *Pseudomonas*, and *Agrobacterium*.

Here, we propose this new simple workflow for rapid Spittlebugs froth bacteria identification via MinION sequencing, reducing the time and providing a reliable method applicable to anaerobic and microaerobic conditions.

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# A New Approach in Electrochemical Biosensing Technology Using 3D Printed Carbon Electrodes

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## Abstract

3-dimensional printing (3DP) technology is gaining importance every day because it allows for diversity in design and portable production. 3DP can realize production in a shorter time compared to traditional methods. The fact that it provides the possibility of production in different geometric shapes allows the advantages of various geometries to be used in different bioanalytical applications [1,2]. With the 3D printed working electrodes being produced in our laboratory, it is aimed to pave the way for the development of nucleic acid-based biosensors (genosensors) that can be used in routine analyses for the determination of different biomarkers/molecules in the clinical field. In this study, a FDM 3D printer working with carbon black and PLA-based filament was used to produce sensor surfaces, which we produce as an alternative to the working electrodes of the triple electrode system in electrochemical sensors. In this direction, fish sperm dsDNA and ssDNA oligonucleotide representing *Escherichia coli* bacteria are biomodified to 3DcbE's (for label-free voltametric detection). Differential pulse voltammetry technique is used for label-free detection of hybridization. The nanostructure of the sensor surface was observed by SEM method. And then an electrochemical aptasensor design was carried out for the rapid, specific and reliable determination of the Myelin Basic Protein (MBP) molecule, which is a biomarker of multiple sclerosis (MS) disease [3]. In addition, the Drug-DNA Interaction with 3DcbE's has also been analyzed using doxorubusin, and it has been shown that the guanine oxidation signal decreases after the interaction of DNA and DOX. It is envisaged that the functionalization and modulation of the structural properties of CB/PLA electrodes will provide new possibilities for the immobilization of materials with electrocatalytic properties, thereby allowing the detection of a wide range of analytes.

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## Figures

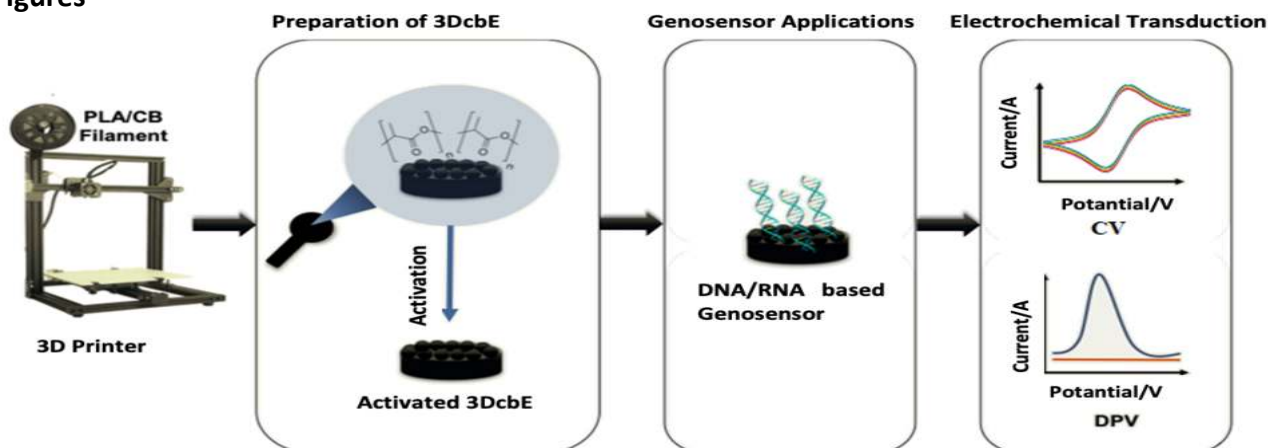


Figure 1: Schematic presentation of the study procedure

# Integrating nanotechnology with mercuric reductase from bacteria for enhanced mercury bioremediation

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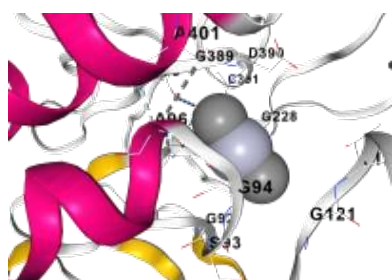
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Mercury (Hg) pollution is a significant environmental issue due to its toxic effects, persistence, and ability to bioaccumulate in ecosystems, posing serious risks to both human health and wildlife. This study focuses on the mercuric reductase enzyme from the *Pseudomonas fluorescens*, which is crucial for mercury detoxification. The enzyme reduces toxic mercury ions ( $\text{Hg}^{2+}$ ) into less harmful elemental mercury ( $\text{Hg}(0)$ ), thus mitigating mercury's harmful impacts. Bioinformatics tools were used to analyze the enzyme's protein sequence to understand its structural and functional characteristics. Virulence prediction confirmed that the enzyme is non-toxic and non-pathogenic. Further analysis, including homology modeling and docking studies, provided detailed insights into the enzyme's three-dimensional structure and its interactions with mercury substrates. The mercuric reductase enzyme, belonging to the Pyridine nucleotide-disulphide oxidoreductase family, class I, is composed of 548 amino acids and contains crucial functional domains necessary for mercury reduction. Physicochemical analyses revealed that the enzyme is hydrophilic and structurally stable. The predicted three-dimensional model was validated, confirming its accuracy. Evolutionary studies identified conserved regions among homologous sequences, suggesting functional relationships with other mercury-detoxifying proteins. Additionally, protein-protein interaction networks highlighted the enzyme's collaborative role in mercury detoxification pathways. Docking studies further demonstrated the enzyme's efficacy in reducing mercury. The study also explores the integration of nanotechnology to enhance the enzyme's activity and stability. Nanoparticles can serve as carriers, improving enzyme immobilization and facilitating targeted delivery, thereby increasing the efficiency of mercury bioremediation. This innovative approach could significantly boost the effectiveness and sustainability of mercury pollution management strategies. In conclusion, the combination of mercuric reductase from bacteria and nanotechnology represents a promising strategy for the eco-friendly remediation of mercury-contaminated environments. This synergy could provide more effective and sustainable solutions for managing mercury pollution, making it an area of interest for further research to optimize its application in various environmental conditions.

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**Figure 1:** A docked complex of dimethyl mercury with mercuric reductase



# Inkjet Printing for Advanced Electrode Fabrication: Precision, Efficiency, and the Role of Graphene-Based Materials in Electrochemical Applications

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Inkjet printing has emerged as a versatile and powerful alternative to traditional methods for modifying working electrodes, particularly in electrochemical applications. This technique provides precise control over material deposition, allowing for the fabrication of highly reproducible and customized electrode surfaces. Unlike conventional approaches like drop casting, spin coating, or photolithography, inkjet printing supports layer-by-layer assembly, enabling the integration of complex, multi-material structures with nanometer precision. Additionally, it minimizes material waste, reduces fabrication time, and preserves the integrity and functionality of sensitive components like nanomaterials and biological molecules.

Compared to traditional printing techniques like screen-printing, inkjet printing offers significant advantages in resolution, material efficiency, and flexibility. It is compatible with a wider range of substrates, making it ideal for rapid prototyping of electrode designs.

A major advancement in inkjet-printed electrodes is the use of graphene derivatives functionalized with specific chemical groups or graphene-based materials engineered at the single-atom level. This allows for precise surface modifications, tailoring electrodes for specialized applications such as biosensing. For example, it enables the attachment of bio-relevant molecules like antibodies or aptamers, improving their functionality in targeted sensing. Single-atom engineering further enhances the performance of graphene by precisely positioning atoms within the lattice, greatly boosting catalytic activity, electrical conductivity, and surface area.

# Selective determination of bortezomib with a plant-based nanoflower-modified electrochemical MIP sensor

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Bortezomib (BOR) is the first developed proteasome inhibitor and is used to treat multiple myeloma, mantle cell lymphoma, and gastrointestinal stromal tumors [1,2]. This study reports the design of a molecularly imprinted polymer (MIP)-based electrochemical sensor using green-synthesized saffron-based copper nanoflowers (CuNFs) to selectively and sensitively determine BOR in biological and pharmaceutical samples. The MIP structure was fabricated on the glassy carbon electrode (GCE) surface via the photopolymerization process (365 nm UV light, 190 min). The MIP components include template drug BOR, functional monomer 2-Acrylamido-2-methyl-1-propane sulfonic acid (AMPS), cross-linker, basic monomer, initiator, and CuNFs for improved porosity. Factors affecting the MIP design (nanoflower type and amount, functional monomer ratio, dropping volume, removal and rebinding processes) were optimized step by step. Electrochemical and morphological characterization studies for MIP-based sensor surfaces and CuNFs were performed by scanning electron microscopy (SEM), energy dispersive X-ray analysis (EDX), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), atomic force microscopy (AFM), cyclic voltammetry (CV), and electrochemical impedance spectroscopy (EIS) techniques. The developed sensor gave a linear response for the standard solution and serum sample in the 0.25 – 2.5 pM concentration range. The limit of detection (LOD) and limit of quantification (LOQ) values were between 29 and 169.3 fM. The recovery analysis in serum and injection powder samples proved the sensor's applicability and accuracy. Furthermore, selectivity studies using four metabolites of BOR demonstrated the sensor's superior selectivity performance. Additionally, the interference-free performance was confirmed even in the presence of a 1000-fold concentration of interference agents. Consequently, this newly developed sensor can be used as an advantageous method for highly selective, sensitive, and reliable determination of BOR.

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# Multiparameter Monitoring of Oral Health Biomarkers Using Integrated Flexible Sensors

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Maintaining optimal oral health relies on a comprehensive understanding of the intricate bio-adhesive, bio-mineralization, and metabolic processes occurring within the oral cavity. These processes are significantly influenced by the complex composition of oral fluids, particularly saliva and its resident microbiome. [1],[2] However, traditional methods struggle to capture the dynamic fluctuations and heterogeneous variations in oral biomarkers. [3],[4]

This paper presents a novel approach for continuous, real-time monitoring of multiple oral health biomarkers using integrated flexible sensors embedded within a personalized dental splint. The device incorporates electrochemical and open circuit potentiometry sensors to measure key parameters such as glucose, pH, lactate, calcium, phosphate, and fluoride concentrations in saliva, alongside monitoring real-time biofilm formation.

As an example, the pH measurements are presented. The pH sensors exhibited a linear response of -53.8 mV/pH in buffer tests. Unstimulated saliva samples from different volunteers were measured, and the pH values matched closely with those obtained using a commercial pH electrode. Potentiometric measurements were also conducted for calcium and fluoride ions.

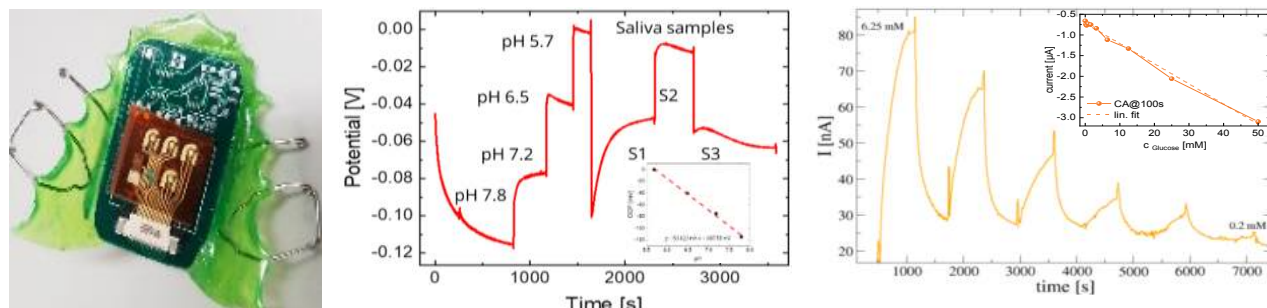
Continuous glucose and lactate monitoring was achieved amperometrically, demonstrating the platform's potential for real-time tracking of key metabolic markers.

This multi-sensor platform offers a promising avenue for early detection of oral diseases, personalized treatment strategies, and improved patient outcomes.

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## Figures



**Figure 1:** a) Device for continuous monitoring of health parameters within the oral cavity. b) Potentiometric measurement of pH. Shown are measurements with phosphate buffers of the indicated pHs and measurements with three different saliva samples. (b) Amperometric response of glucose sensors.

# Rhodamine B Decomposition in Water Using Metal-Doped TiO<sub>2</sub> Photocatalysts supported on Zeolite or Nano-Graphite Substrates

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Rhodamine B is widely employed in the dyeing of paints, acrylics, textiles, and biological products, but its direct discharge into water can pose significant toxicity risks to organisms. This paper reports the findings on the degradation of Rhodamine B in water into environmentally benign products, using metal (Me)-doped TiO<sub>2</sub> (pure anatase) photocatalysts supported on zeolite or nano-graphite substrates. The TiO<sub>2</sub> synthesis process involved an innovative sol-gel technique combined with microwave treatment, leading in the production of highly pure anatase (TiO<sub>2</sub>). These materials and involved processes demonstrate significant potential for purification of water from organic pollutants. Comprehensive materials characterization was conducted using Scanning Electron Microscopy (SEM), Fourier Transform Infrared Spectroscopy (FTIR), Scanning Transmission Electron Microscopy (STEM), and X-ray Diffraction (XRD) techniques.

# Plasma-Treated and Doped WS<sub>2</sub> Nanoparticles for Energy Applications

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Multiwall WS<sub>2</sub> nanotubes and polyhedral fullerene-like nanoparticles were discovered in the earlier 1990s. An efficient synthesis method for the scaled-up production of high purity inorganic fullerene WS<sub>2</sub> nanoparticles was later developed, which allows to produce tens of kilograms per day. The availability of these nanomaterials led to investigation of their properties, and stimulated numerous applications in energy related applications, some of them have been recently investigated by us and include hydrogen storage [1], electrocatalysts [2], and solar cells [3].

We developed a new method of surface modification of WS<sub>2</sub> nanotubes through cold radiofrequency (RF) plasma for hydrogen evolution reaction (HER). The effect of plasmatic ions on WS<sub>2</sub> nanotubes has been investigated. The plasma-treated samples showed improved performances in HER electrocatalysis. Both Ar and D<sub>2</sub> RF plasma treatments, when performed separately, show similar effects on electrocatalysis performances with improved HER overpotentials of ~340 mV at 10mA/cm<sup>2</sup> compared to 567 mV of the pristine WS<sub>2</sub> nanotubes, whereas the combined treatment by Ar and then by D<sub>2</sub> RF plasma notably decreased the overpotential to 264 mV.

Additional, currently developed application of WS<sub>2</sub> nanoparticles is to integrate them in perovskite solar cells (PSCs). Photoinduced degradation, thermal effects, and chemical reactions result in degradation of such PSCs. Using our currently developing approach we aim to overcome their instability by developing the novel hybrid PSC/MS<sub>2</sub> nanocomposites, as shown in Fig. 1. MS<sub>2</sub> (M = W or Mo) nanotubes are capable of absorbing a wide range of visible light and are very stable. Combining MS<sub>2</sub> nanotubes and perovskites can increase the stability of so produced composite. As MS<sub>2</sub> nanotubes support polaritonic modes at room temperature, they are optically active in Vis and NIR-IR regions and so can be utilized for light absorption and emission across this spectral range. The composites of perovskites/MS<sub>2</sub> nanotubes offer an additional benefit of charge transfer. For this purpose, they are being exposed to focused ion beams to induce Ga implantation so achieving the improvement of their conductivity and decrease of the band gap [4].

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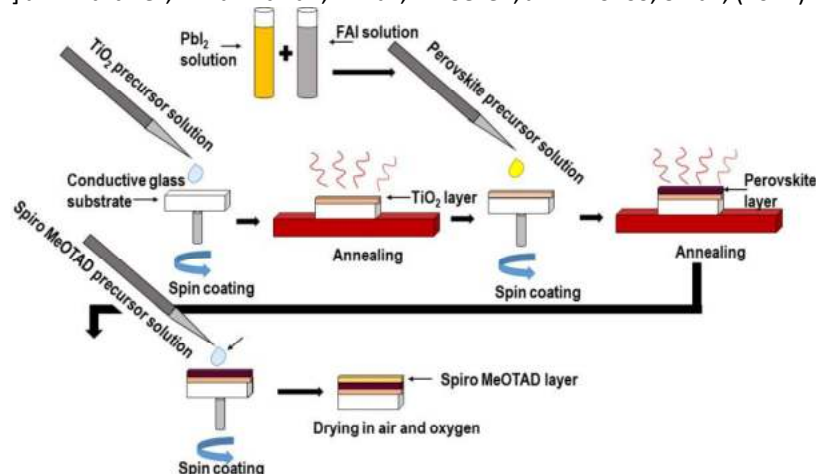


Figure 1: Schematic view of the steps in the WS<sub>2</sub>/PSC assembly.

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Vitiligo is a long-term skin condition that leads to the loss of pigmentation in both the skin and hair, and it severely impact on patients' quality of life who suffer from it [1]. Currently available treatments, both topical and systemic, are often ineffective due to the skin barrier properties and the way drugs are metabolized or inactivated. This has led researchers to explore the use of ultradeformable nanomedicines as a potential treatment. Khellin is a natural active ingredient that has shown potential in the treatment of vitiligo, but its physico-chemical properties strongly limit its skin permeation as free form [2]. Considering the impairment of the antioxidant pathways as co-factors in vitiligo skin disorder, the goal of this study is to create nanocarriers that could deliver both khellin and idebenone through the skin. Nanocarriers were assessed for their physicochemical properties, i.e. size, distribution, zeta potential, stability, entrapment efficiency. Ethosomes made up of 1% w/v Phospholipon 90G and 30% ethanol, along with transfersomes, were identified as having the most favourable features for cutaneous application and were chosen for further in vitro testing. Skin permeation studies using human stratum corneum and epidermis showed that transfersomes provided better permeation, enhancing the delivery of both khellin and idebenone. The effectiveness of the realised nanomedicines was investigated considering an in vitro model of vitiligo, using human melanocytes pre-treated with hydrogen peroxide. Results indicated that nanocarriers containing khellin and idebenone helped in restoring pigmentation. Further in vitro testing performed on human healthy volunteers confirmed the great safety of the realised nanocarriers, suggesting their potential clinical use. Overall, our study demonstrated the adaptability of the vesicular nanosystems in delivering a combination of two active compounds, an antioxidant and furanochromone, that may offer a promising alternative treatment for vitiligo disorder.

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In recent years, biomass has attracted attention as a raw material for sustainable material production [1]. In addition, electro-organic synthesis has attracted attention as a clean technology that does not involve excess reagent waste, as the reaction is initiated by electron transfer on the electrodes. Along these lines, we aimed to convert biomass-derived material into a fuel precursor: electroreduction of furfural to furfuryl alcohol.

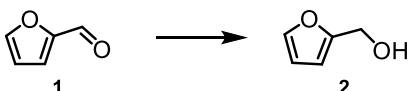
Constant current electrolysis was performed in an undivided batch cell: furfural (**1**; 0.1 M), MeOH (5.0 mL), 0.50 mA/cm<sup>2</sup>, 400 rpm, and rt. Supporting electrolytes, electrode materials, and the amount of charge (referring to **1**) were screened to optimize reaction conditions. Products were identified by gas chromatography-mass spectrometry (GC-MS).

Electroreduction of **1** produced furfuryl alcohol (**2**). The highest GC-MS yield of **2** was 21% under optimum conditions: (anode) graphite, (cathode) boron-doped diamond (BDD), (supporting electrolyte) KOH (0.15 M), (current density) 2.0 mA/cm<sup>2</sup>, and (amount of charge) 4.0 F (referring to **1**) (**Table 1**, entry 8). For a supporting electrolyte, not only the inorganic salt (KOH) but also the organic salt (Bu<sub>4</sub>NOH) was investigated, indicating that the size of cation species of supporting electrolytes affects the yield of **2**. It is noted that this tendency is also observed in the previous study of microflow electrolysis of **1** [2]. In terms of the amount of charge, GC-MS yields were high when the amount of charge was greater than 2.0 F. Since the present reaction is assumed to be a two-electron reaction, it is suggested that a side reaction to afford 2-furoic acid methyl ester (**3**) is proceeded (**Scheme 1**).

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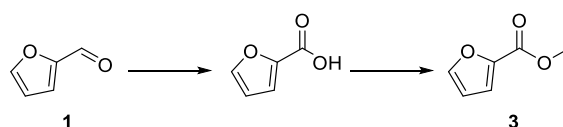
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**Table 1.** Screening of reaction conditions.



Electrode, Supporting electrolyte, Amount of charge (referring to **1**), Current density, MeOH, rt.

Entry	Electrode Anode / Cathode	Supporting electrolyte	Amount of charge (referring to <b>1</b> )	Current density	GC-MS yields	
					<b>1</b> / %	<b>2</b> / %
1	Cu / BDD	Bu <sub>4</sub> NOH	2.0 F	2.0 mA/cm <sup>2</sup>	43	4
2	Cu / BDD	KOH	2.0 F	2.0 mA/cm <sup>2</sup>	36	13
3	Graphite / BDD	KOH	2.0 F	2.0 mA/cm <sup>2</sup>	28	15
4	Graphite / BDD	KOH	1.0 F	2.0 mA/cm <sup>2</sup>	21	13
5	Graphite / BDD	KOH	4.0 F	2.0 mA/cm <sup>2</sup>	30	18
6	Graphite / BDD	KOH	4.0 F	0.50 mA/cm <sup>2</sup>	37	21



**Scheme 1.** Plausible side reaction in the electroreduction of furfural (**1**).

# Monitoring Volatile Organic Compounds in Indoor and Outdoor Air Using Passive Sampling in Milan, Italy

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Volatile organic compounds (VOCs) are significant contributors to urban air pollution, affecting both human health and environmental quality [1]. This study aimed to monitor VOC levels in indoor and outdoor environments at five locations in Milan, Italy, over a two-month period during the summer of 2024, a time characterized by high emissions and intensified photochemical activity. Using Radiello® passive samplers and gas chromatography-mass spectrometry (GC-MS), the VOC concentrations were measured and the emission profiles of household cleaning and personal care products were analysed to assess their impact on indoor air quality. The results showed that the average total VOC concentration (TVOCs) outdoors was  $220.8 \pm 195.4 \mu\text{g}/\text{m}^3$ , while indoor levels were slightly higher at  $243.6 \pm 134.3 \mu\text{g}/\text{m}^3$ , resulting in an indoor-to-outdoor ratio of  $1.32 \pm 0.719$ . These concentrations surpass typical background levels in other European cities [2], underscoring the complex nature of VOC emissions in Milan. The most abundant VOC group in both environments were alkanes, although their relative distribution differed. Outdoors, the predominant groups were alkanes > aromatic hydrocarbons > alkenes > terpenes > esters > alcohols & ethers > halogenated compounds > organosiloxanes > aldehydes & ketones. Indoors, alkanes and terpenes were dominant, followed by esters, alcohols & ethers, aromatic hydrocarbons, and other compounds. To further assess the dynamics of VOCs, the (*m* + *p*)-xylene to ethylbenzene (X/E) ratio was employed as an indicator of photochemical aging [3, 4]. Notably, the recommended indoor TVOC threshold of  $200 \mu\text{g}/\text{m}^3$ , established by Møhlhave to minimize discomfort and health risks, was exceeded in three out of four monitored apartments.

## Acknowledgments

We express our sincere gratitude for the funding provided by the European Commission under the project titled “Nanoparticles in Environment and Medical Research” (NanoKos - 438247).

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# Electrochemical Measurement of Antiglaucoma Drug Brimonidine Using Boron-Doped Diamond Microelectrodes

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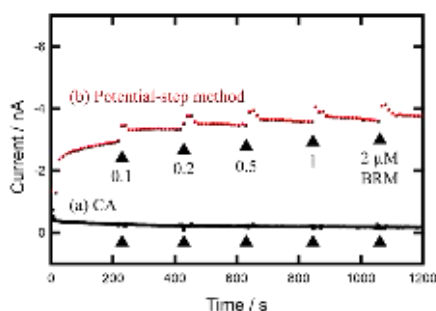
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Glaucoma is the leading cause of blindness in Japan [1]. The standard treatment for glaucoma is to lower intraocular pressure with eye drops, but there are still many unknowns regarding intraocular pharmacokinetics. Here, we proposed an electrochemical method using boron-doped diamond (BDD) electrodes to observe changes in intraocular drug concentrations over time. BDD shows excellent electrochemical properties and biocompatibility [2], allowing it to be applied as a sensor for measuring drugs *in vivo*. In this study, we performed the electrochemical measurements of the popular antiglaucoma drug brimonidine tartrate (BRM). Firstly, the electrochemical properties of BRM were evaluated by cyclic voltammetry (CV) measurements using a three-electrode configuration: a BDD plate electrode as the working electrode (WE) and the counter electrode (CE), and an Ag/AgCl (sat. KCl) electrode as the reference electrode (RE). In CV measurement, a reduction signal of BRM was observed at -0.4 V and below. Subsequently, we performed continuous measurements using a BDD microelectrode as WE. Chronoamperometry (CA) measurements applying -0.5 V showed highly linear concentration dependence in phosphate buffer but not in aqueous humor (Fig. 1 (a)). The adsorption of biological materials to the surface of the electrode was thought to be the primary cause of this degradation in the sensor's sensitivity. To address this, a potential-step method (consisting of -0.2 V applied for 29.5 s and -1.5 V for 0.5 s) was established. This method includes a phase where a particular potential (-0.2 V) is applied, which induces no electrochemical reaction on the electrode surface, thereby preventing adsorption. By using this method, a reduction signal of BRM in aqueous humor was observed (Fig.1 (b)). The optimized potential-step method was applied to *in vivo* measurements with anesthetized mice. The BDD microelectrode was inserted into the right cornea. CE and RE were placed on the surface of the left eye. 5  $\mu$ L of 6 mM BRM was administered to the right eye. The reduction signal of BRM started to increase  $\sim$ 2 min after the administration (Fig. 2). The signal returned to the original level 17 minutes after administration (Fig. 2). This result indicates the possibility of *in vivo* monitoring of drug concentration changes in the eye.

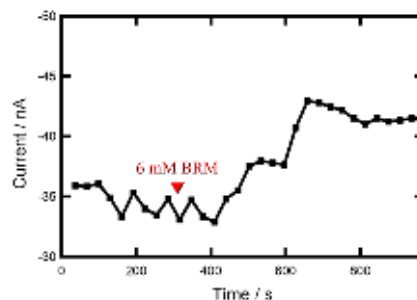
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## Figures



**Figure 1:** Continuous measurements in aqueous humor, (a) CA (b) potential-step method.



**Figure 2:** *In vivo* measurements with mice (moving average of 2 intervals).

# Current approaches based on electrochemical DNA nanobiosensors for genetic diagnosis or analysis of drug-DNA interactions

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## Abstract

Since the first commercial biosensor was introduced to the market for blood glucose measurement in the seventies, many different types of biosensors have been developed up to now. Biosensor R&D studies are still popular around the world. In some global biosensor reports that include a large number of literature and industry-based data published recently, it is predicted that handheld/portable or wearable biosensors will be preferred in many areas of analysis such as food, medicine, agriculture, etc. in the very near future.

The new generation of biosensors developed with nanomaterials, which have been used in the field of biosensors for many years and still maintain their important place in the scientific world today, have played a key role in the development of many sensitive devices. Among these nanoparticles, carbon-containing species are considered to be particularly valuable in electrochemical biosensor designs due to their cost-effective analysis, good conductivity properties, and ease of use.

In this direction, information is provided about some current electrochemical nanobiosensors and biosensor-based diagnostic kits and their analysis performances designed in our laboratory for genetic disease or drug-DNA interaction analysis in recent years.

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# Molecularly Imprinted Polymers (MIPs) as Synthetic Antibodies for Inhibiting SARS-CoV-2 Omicron Variant

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Emerging zoonoses, which are infectious diseases transmitted from animals to humans, present significant public health challenges due to their potential for widespread outbreaks, requiring prompt and effective therapeutic responses, as seen with COVID-19. In this context, the present study focuses on advancing the technology used to prepare Molecularly Imprinted Polymers (MIPs), which act as synthetic antibodies targeting specific molecules involved in zoonotic diseases [1].

Following docking simulations, MIPs designed to specifically target the Receptor-Binding Domain (RBD) of SARS-CoV-2, with a focus on the Omicron variant, were prepared (Fig. 1). The synthesis was performed via inverse microemulsion polymerization, and the resulting MIPs were characterized by DLS,  $\zeta$ -potential, TEM (Fig. 1A) and NTA analyses. Building on previous research [2], the process conditions were modified to improve particle stability and achieve better control over size and distribution, addressing limitations observed in earlier studies.

The selective recognition properties of MIPs and their ability to block the interaction between ACE2 and the RBD of SARS-CoV-2 were investigated *in vitro*, using Non-Imprinted Polymers (NIPs) as control materials, and binding studies were carried out using a Quartz Crystal Microbalance with Dissipation monitoring (QCM-D).

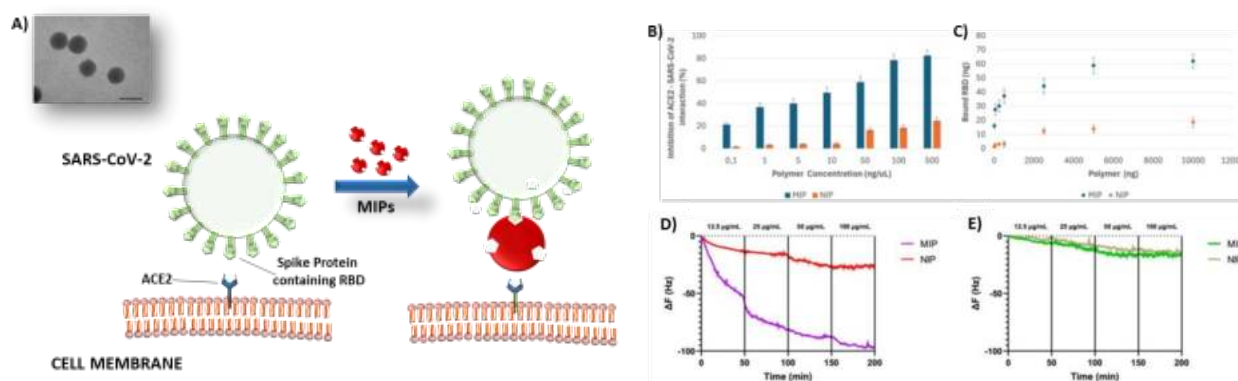
The prepared imprinted nanoparticles were monodisperse with an average diameter of  $40.24 \pm 6.383$  nm and a  $\zeta$ -potential of  $-33.3 \pm 8.14$  mV. The nanoparticles showed significant recognition properties and a concentration-dependent ability to reduce RBD binding to its receptor ACE2 (Fig. 1B-1E), suggesting they can effectively inhibit this interaction and, thus, the infection process. In addition, the synthesized MIPs exhibited no cytotoxicity or sensitizing effects, as evaluated by MTT and h-CLAT assays.

MIPs-based antibodies offer a promising alternative to natural antibodies for SARS-CoV-2 treatment, providing a versatile platform for addressing emerging zoonotic diseases.

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## Figures



**Figure 1:** MIPs-based antibodies: **A)** TEM; **B)** inhibition of ACE2-RBD interactions; **C)** binding isotherms; real-time changes in resonant frequency ( $\Delta F$ ) on functionalized QCM-D sensor chips with **D)** RBD and **E)** HSA.



# 3D-printed microneedle-based electrochemical sensing devices for plant health assessment

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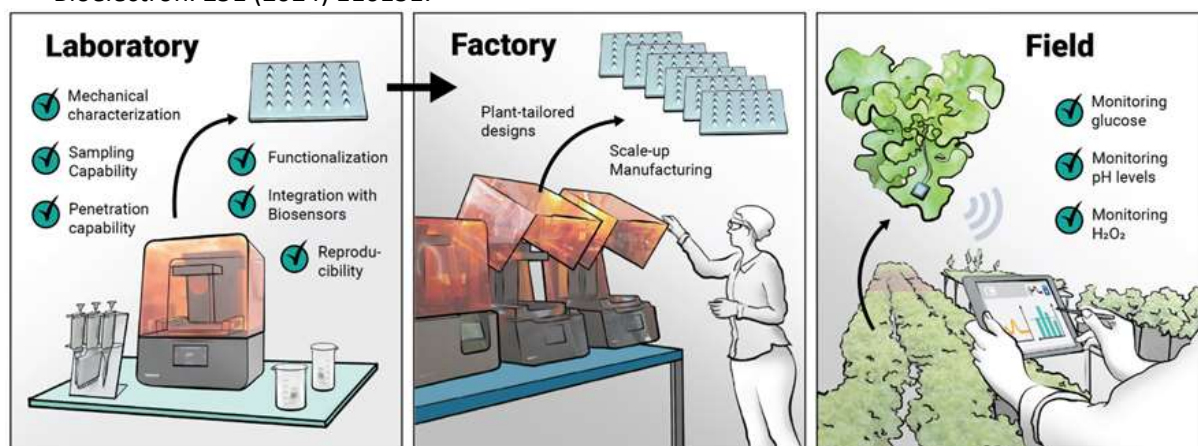
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Plant health monitoring is devised as a new concept to unravel real-time physiological processes such as plant stress signaling [1]. The need for an increasing food supply due to an increment in the worldwide population does not match the dramatic effects of climate change, which hinders crop health and increases plant stress. Therefore, plant stress scavengers such as wearable sensors could play a role in controlling crop health and adaptation to new climates [2]. However, affordable sensing devices need to be developed to bring smart sensors into the field. Herein, we propose a technological platform based on a low-cost 3D-printed hollow microneedle array patch (HMA) as a sampling device coupled with biosensors based on screen-printed technology to develop affordable smart sensors for in situ plant analysis [3]. First, an optimization of the 3D-printing method showed for the first time a tip diameter of  $25.9 \pm 3.7 \mu\text{m}$  using a 3D printer (<500 EUR) based on stereolithography. Notably, the HMA withstands the forces exerted by thumb pressing (i.e. 20-40 N) needed for a proper insertion. Subsequently, the holes of the HMA enabled up to 15  $\mu\text{L}$  of fluid extraction tested in vivo in plant leaves. Importantly, a paper-based sampling strategy adapted to the HMA allowed the collection of plant fluid in leaves. Finally, integrating the sampling device onto biosensors facilitates the in situ electrochemical analysis of plant health biomarkers (i.e.,  $\text{H}_2\text{O}_2$ , glucose, and pH) and the electrochemical profiling of plants. Overall, the design of the affordable electrochemical platform brings a leap forward in versatile sensors for plant (bio)chemical monitoring, which can accelerate the developments in future precision farming.

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**Figure 1:** From the fabrication of affordable microneedle arrays to the sensing application.



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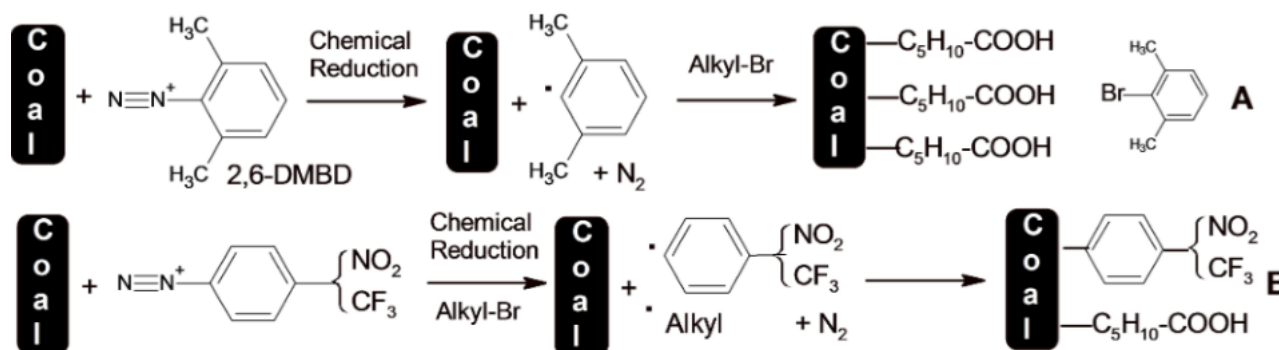
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The use aryl diazonium salts to attach the surface of many materials is now considered a successful alternative to create nanocomposite materials. [1] Their reduction reaction can be triggered in several ways, including electrochemical, chemical and spontaneous reduction which allows the generation of very reactive species, aryl radicals, part of which react with the surface of material and forms an organic layer strongly attached. Another part of these radicals can initiate other reactions in the solution, such as the removal of hydrogen atom from the solvent or halogen atoms from alkyl halides and allow the formation of alkyl radicals, which, at their turn, attach to the material surface. [2,3,4] In this case, mixed alkyl-aryl layers are grafted onto the material surface. When aryl diazonium salts bearing methyl groups ortho to the position to the diazonium group are used, the aryl radicals generated are particularly important because they do not attach to the material surface but can remove halogen atoms from alkyl halides and allow the grafting of alkyl layers. Here we show the results we have obtained with 2,6-dimethylbenzen diazonium salt (2,6-DMBD), which is used to generate 2,6-dimethylphenyl radicals that do not attach to the coal surface due to steric hindrance but are prone to remove bromine atoms from 6-bromohexanoic acid and tether the coal surface with hexanoic groups, scheme 1A. [5] When other diazonium salts are used, we have modified the coal surface with alkyl-aryl layer, scheme 1B. The presence of organic layer is attested with IR and XPS Spectroscopies while DFT calculations are used to calculate the bond dissociation energy.



Scheme 1. A) Chemical reduction of 2,6-DMBD and the formation of alkyl radicals that attach to the lignite surface; B) Reduction of an aryl diazonium salt without steric hindrance i) leads to aryl radicals and ii) also create alkyl radicals, Alkyl\*, both radicals attack the lignite surface to give a mixed. [5]

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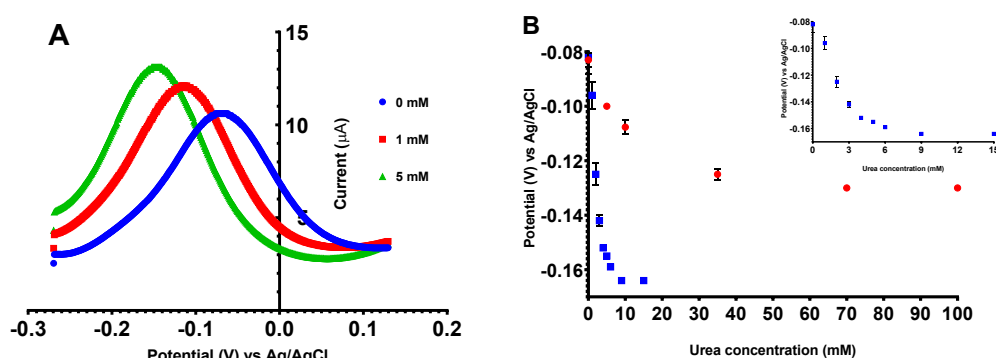
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Since the invention of dialysis, patients with renal diseases have benefited from a noticeable increase in both quality of life and life expectancy due to the continuous progress of this therapy. In 1985, a group of researchers led by Gotch and Sargent introduced a parameter with the objective of assessing the adequacy of dialysis:  $Kt/V$  [1]. During this therapy, the concentration of uremic toxins in blood decreases exponentially.  $Kt/V$  is correlated with the concentration of urea in plasma pre- and post-dialysis and represents the exponential coefficient related to urea clearance. The efficiency of filtration also varies with molecular size, and urea is considered the ideal marker for assessing the removal of small molecules. For these reasons monitoring urea concentration in dialysate ensures effective hemodialysis and helps healthcare providers adjust treatment for optimal results. In this work, an enzymatic electrochemical biosensor for the detection of urea is proposed. The system, which requires minimal sample pretreatment, makes use of urease, a NAD/FAD independent enzyme, and a pH sensitive indoaniline derivative, can be used to perform live measurements in both dialysate or blood during treatment. The sensing mechanism is relatively simple. The ammonia, produced from the breakdown of urea by urease, originates a local variation of pH that is first measured by assessing the shift of the indoaniline derivative peak in square wave voltammetry (figure A), and then correlated to the urea concentration. Sensors with different dynamic ranges can be fabricated by varying the amount of enzyme during production (figure B), allowing sensor use in matrices with different concentration levels of the target analyte.

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## Figures



**Figure 1:** (A) Square wave voltammeteries in PBS at varying concentrations of Urea. (B) Calibration curves of two sensor fabricated using different amount of enzyme

# Impedimetric aptasensor for the determination of patulin mycotoxin with levan modified electrodes

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## Abstract

Mycotoxins are toxic compounds produced by various fungi that grow on a variety of foodstuffs, especially under warm and humid conditions. These toxins can contaminate foodstuffs in the crops or under storage conditions and can pose significant risks to human and animal health if consumed. These mycotoxins can pose a health risk by consuming contaminated cereals, nuts, fruits and spices [1]. Patulin is a mycotoxin produced by fungi belonging to *Penicillium*, *Aspergillus*, and *Byssoschlamys* genera. Patulin is most commonly found in apple products such as apples, apple juice and cider, but can also be found in other fruits, vegetables and foods made from them [2]. Patulin causes harmful effects especially on the gastrointestinal system. In addition, animal studies have reported that patulin causes immunosuppression, neurotoxicity and genotoxicity [3]. This mycotoxin is of global concern as it affects food safety, reduces crop yields and has negative economic and health impacts. Therefore, monitoring and controlling mycotoxin levels in foods is very important for the protection of public health. In this study [4], impedimetric aptasensor developed for the determination of patulin. The surface of the pencil graphite electrode was modified with levan and then the patulin-specific aptamer was immobilized on this surface. After the interaction of aptamer and patulin, measurements were performed by electrochemical impedance spectroscopy technique. Various parameters such as aptamer concentration, immobilization time, interaction time were optimized. The selectivity of the developed aptasensor was investigated against fumonisin B1, ochratoxin A and deoxynivalenol. In order to demonstrate the application of the developed aptasensor, patulin determination was carried out in apple juice, limit of determination was calculated and recovery study was performed.

**Key words:** Patulin, Levan, Aptasensor, Electrochemical impedance spectroscopy, Apple juice

**Acknowledgements:** Arzum Erdem Gürsan would like to express her gratitude to the Turkish Academy of Sciences (TÜBA) as the Principal member for its partial support.

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# Acute exposure to ambient fine particulate matter (PM<sub>2.5</sub>) extracted from Prishtina and Obiliq urban area induces cardiac electrophysiological changes in rats

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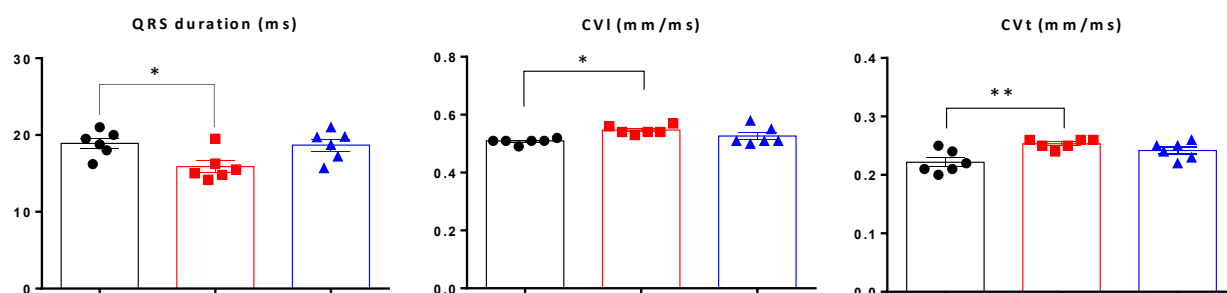
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Air pollution is considered a risk factor for developing cardiac arrhythmias [1]. At the University of Parma, Department of Surgery and Medicine, we have conducted a series of *in vivo* experiments using Sprague Dawley rats as a model to measure the electrophysiological changes that happen to cardiac tissues when they are exposed to PM<sub>2.5</sub> originating from two different cities of Kosovo: Prishtina and Obiliq. Particles were extracted using an established protocol [2]. Rats were exposed through intra-tracheal instillation to saline solution (control group, n=6) or to saline solution plus Prishtina and Obiliq PM<sub>2.5</sub> [2mg/kg] (exposed groups, n=6). After 4h, extracellular epicardial potentials were measured using a 5.5mm x 5.5mm, 11 row x 11 column, 121 lead electrode array placed on the anterior surface of the ventricles in the *in situ* rat hearts. We assessed: 1. Excitability of the cardiac tissue in the context of Rheobase and Chronaxie; 2. Electrograms wave and interval durations; 3. Conduction velocity evaluated longitudinally (CV<sub>l</sub>) and transversally (CV<sub>t</sub>) to epicardial fiber direction by means of isochrone maps; 4. Effective Refractory Period (ERP) using S1-S2 protocol. Statistical analysis was performed using GraphPad Prism 6.0 and data were tested using one way Anova. QRS duration was decreased in the Prishtina group compare to control, while CV<sub>l</sub> and CV<sub>t</sub> were increased in the Prishtina group. No statistically significant changes were observed in the Obiliq group. This study emphasizes the impact of air pollution on cardiac tissue and could contribute to making better public policies toward a greener environment.

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## Figures



**Figure 1:** Bar graphs showing the changes in QRS complex duration, conduction velocity evaluated longitudinally (CV<sub>l</sub>) and transversally (CV<sub>t</sub>) to epicardial fiber direction between control group (black) and exposed groups (Prishtina, red; Obiliq, blue). \* p<0.05 \*\* p<0.01

# Kinetics of bromophenol blue oxidation on carbon felt anode and anode induced graphene oxide nanoparticles

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## Abstract

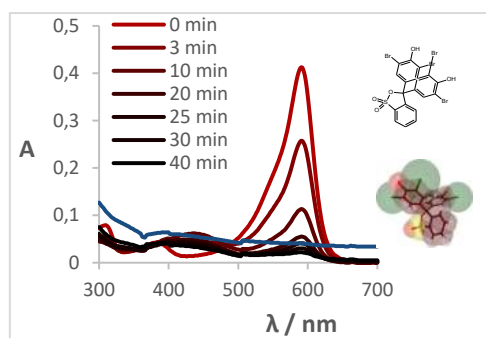
Electrochemical oxidation of organic pollutants is a very effective method for polluted water treatment. It is based on the electron transfer from the pollutant molecule to the anode, and mostly on the pollutant oxidation by oxidant species generated on the anode and the cathode, such as  $\cdot\text{OH}$ ,  $\text{H}_2\text{O}_2$ , and  $\text{S}_2\text{O}_8^{2-}$  [1,2]. Carbon felt (CF) is widely used as a cathode contaminated water treatment, but its use as an anode is less explored [1,3,4]. Bromophenol blue (BPHB) was oxidized in an electrolytic cell with CF as both anode and cathode, and  $\text{Na}_2\text{SO}_4$  as supporting electrolyte, at various current intensities and supporting electrolyte concentration. During the electrolysis, graphene oxide nanoparticles were generated from the anode, which also are expected to be involved in the oxidation and adsorption of BPHB. At the beginning of the electrolysis, a small increase in the cell voltage was observed, then it reached a plateau or decreased slightly. The concentration of the BPHB during the electrolysis was monitored by UV-Vis spectrophotometry. The oxidative degradation of BPHB was very quick and the rate of degradation increased with lowering  $\text{Na}_2\text{SO}_4$  concentration and increasing current intensity.

**Keywords:** Carbon felt, nanoparticles, electrochemical oxidation, bromophenol blue.

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## Figures



**Figure 1:** UV-Vis spectrum evolution during BPHB oxidation in a CF/CF electrolytic cell. [BHPB] = 0.01 mM,  $i$  = 25 mA,  $[\text{Na}_2\text{SO}_4]$  = 1 mM.

## AI-Enhanced Optical and Electrochemical Biosensing for High-Throughput Plant Phenotyping: From Nano-Scale to Whole Plant Analysis

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A method using automated hardware and software approaches for phenotyping model plants in multiple environmental conditions will be presented. Multi-trait high-throughput screening, which can test higher tens of variants in one experimental run (in total >25,000 plants), uses simple RGB imaging of Arabidopsis in controlled conditions. The variants represent combinations of concentration ranges of tested chemicals/products, genotypes, individual abiotic stresses (water and nutrient limitation, salinity, heavy metals), individual biotic stresses (Botrytis, Pseudomonas), and their multiple combinations. The tested agents can be applied through seed/seedling priming or root absorption. The methodology is powered by the use of an artificial intelligence model to identify plants within images, followed by the extraction of numerous parameters such as the area of the plant, its perimeter, and a detailed colour description. These parameters are automatically evaluated through a Python script, facilitating a standardized, comprehensive analysis of various phenotypic traits, including growth dynamics and morphological and stress response traits. Incorporating statistical analysis into the data processing is planned to evaluate the acquired data thoroughly. We aim to improve our phenotyping method by integrating electrochemical sensors for online monitoring of the chemical signals in and around the plants, allowing for continuous monitoring of critical parameters in plant physiology. This can help expand phenotyping methods to develop a robust system for selecting new technologies and plant varieties more resilient to environmental stressors.



# Functionalization of Magnetic Nanoparticles with Tryptophan and Isatin for Enhanced Glioblastoma Treatment

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The dynamic landscape of cancer therapy demands novel approaches for effective diagnosis and treatment [1,2]. This study presents the synthesis of magnetic nanoparticles (MNPs), and functionalized with a unique molecules, Tryptophan (Trp) and isatin, showing affinity to brain components. A comprehensive characterization through the use of SEM-EDS, FTIR, XPS, and DLS techniques provides an in-depth understanding of the physicochemical properties of the nanoparticles. *In vitro* evaluations on U-87 glioblastoma cells examine crucial factors, including cell adhesion, viability, and potential responsiveness to radiotherapy. This research investigates the potential practical applications of Trp-isatin functionalized MNPs in the treatment of glioblastoma. The preliminary findings suggest that MNPs have the potential to serve as multifaceted agents in glioblastoma therapy. The conjugation of Trp and isatin enhances molecular specificity, suggesting new possibilities for targeted treatment. Additionally, the study highlights the capacity of these MNPs to boost the effectiveness of radiotherapy, indicating their potential role as radiosensitizers. This work contributes to the growing field of nanomedicine and holds promise for advancing targeted treatments for glioblastoma, potentially leading to innovative strategies in the ongoing fight against this challenging disease.

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# Development and Characterization of Two Novel Nanomedicine-based Approaches to Restore the Anti-tumor Activity of the Immune System in Glioblastoma Patients

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The tumor microenvironment (TME) plays a pivotal role in cancer progression and treatment response. Glioblastoma multiforme (GBM), is characterized by a highly immunosuppressive TME, that contains a variety of non-neoplastic cells, including a considerable proportion of infiltrating leukocytes, most of which are macrophages representing around 30% of the total tumor mass. Targeting specific cell subsets within the TME in glioblastoma multiforme (GBM), can indeed be beneficial, but it poses several challenges due to the unique characteristics of the brain and the complexity of the TME. Our recent studies highlight that bone marrow-derived macrophages (BMDMs), distinct from resident microglia, accumulate towards the core of GBM lesions and exhibit potent immune suppressive activity [1].

Given the peculiarity of GBM microenvironment, advances in nanotechnology, immunotherapy, and targeted drug delivery systems may offer promising avenues for developing more effective and precise treatments for GBM. Indeed, in our project we combined both the fields of nanomedicine and tumor immunology and developed two novel approaches to modulate the immune response in GBM patients by exploiting innovative controlled drug delivery nanosystems. One is an Oil-in-Water (O/W) nanoemulsion (NEs), prepared using the microfluidic technique. This NE is loaded with Zinc protoporphyrin IX (ZnPPiX), a potent inhibitor of heme oxygenase-1 (HO-1), an enzyme involved in the iron metabolism and immunosuppressive activity of BMDMs [2].

The second nanosystem is a polymeric nanoparticle, prepared using the ionic gelation technique. It is loaded with a derivative of the chemotherapeutic drug oxaliplatin called diaminocyclohexane-platinum II (DACHPt) [3], capable of inducing immunogenic cell death (ICD), a phenomenon that can be detected through the measurement of specific danger-associated-molecular-patterns (DAMPs) like the extracellular ATP and HMGB1 release [4]. Both nanosystems were characterized for their physicochemical properties.

Our results obtained through *in vitro* models and primary cells present in the TME of GBMs, suggest that the ZnPPiX-loaded NEs could be used to target BMDMs and induce their re-programming towards a more pro-inflammatory and anti-tumoral phenotype. Moreover, data regarding the polymeric nanosystem showed that it could be exploited to target both tumor cells and myeloid immunosuppressive cells while inducing ICD.

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### Abstract

Increasing and ongoing investigations on the nanoscale level have put a focus on the necessity to understand the dark side of metallic nanoparticles. Physiological alterations have been described as a negative serious side effect by metals of nanoparticles. The most prominent metal nanoparticles introduced in health sciences, medicine and especially in therapeutical approaches are gold, silver and copper. In the last years, another heavy metal compound that has been applied not only in single use, but also in combination with an accompanying nanoparticle has arisen, zinc nanoparticles. Despite the heavy implementation of nanoparticles in various fields of medicine, there are still unanswered questions about their safety in regard to human health. Studies have associated the use of nanoparticles with inflammation, production of oxidative stress and acute and/or chronic toxicity. Nevertheless, the mechanism of action is not completely understood on how and when nanoparticles transit from being beneficial to harmless. Our investigations focus on the relation between biological physiological abnormalities dependent on type of response, time of exposure, and dosage of the zinc nanoparticle used. Our results show that blood cells treated with zinc nanoparticles up to 4 hours continue to display anti-apoptosis activity, whereas longer exposure induces cell death.

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# Integration of smart nanomaterials with advanced nanotechnology for development of nanosensors for water pollution detection

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## Abstract

Disposable electrochemical sensors have received special attention in recent years due to the advantages they offer in qualitative and quantitative identification of target analytes. Moreover, they are finding important applications in environment monitoring due to their cost-effectiveness for continuous monitoring. The development of sustainable nanosensors for the detection of environmental pollutants (heavy metals, pesticides and antibiotics), has been a key focus of the SUSNANO project, a Horizon Europe Twinning initiative involving various partners. Over two years of implementation, the scientific research work has concentrated on the fabrication of nanosensors by integrating newly synthesized nanomaterials with advanced nanotechnology, facilitated by complementary collaboration among four partners.

Advanced materials such as graphene [1] and its derivatives (GA, GAN, GCN, GN3, GAF<sub>e</sub>, etc.), reduced graphene oxide (rGO), and composites of reduced graphene oxide with metal nanoparticles (gold, silver etc.), [2], have been studied and applied to develop nanosensors for environmental pollutant monitoring. Several printing techniques (screen printing, inject printing, laser scribing etc.) [3, 4, 5], have been employed to fabricate nanosensors, particularly for water monitoring in real-world scenarios in Albania (rivers, lakes)

The successful and comprehensive research conducted within the SUSNANO project has significantly enhanced the scientific and innovation capacity of the University of Tirana. This has resulted in two major achievements: first, the establishment of a fully equipped electrochemical laboratory for the production, testing, and application of electrochemical sensors, and second, the consolidation of a specialized research group dedicated to the fabrication of electrochemical sensors for research and application.

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# Alternative Approaches for Graphene Oxide Synthesis and Their Application in Advancing Electrochemical Methods

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## Abstract

Carbon nanomaterials, such as Graphene Oxide (GOx) and reduced Graphene Oxide (rGO), are increasingly utilized to enhance material properties and as modifiers in chemical sensors for various analyses and monitoring applications. Since graphite, the precursor for synthesizing these nanomaterials, is both inexpensive and readily available—whether sourced industrially or naturally—the primary focus of researchers is to develop the most efficient, cost-effective, and practical methods for converting graphite into these valuable nano-sized materials.

In this study, we employed the modified Hummers method and an electrochemical synthesis method to produce graphene oxide from graphite powder. The resulting products were characterized using several techniques, including electrochemical analysis (cyclic voltammetry, CV), optical spectroscopy (NanoDrop UV-Vis), Zeta potential measurement, and scanning electron microscopy (SEM) to verify their size and uniformity. The aim of the work is to apply these graphene oxides to modify electrodes for the electrochemical degradation and analysis of antibiotics in aqueous solutions.

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# Challenges in Assessing Albanian Wine Quality through Their Total Antioxidant Content

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## Abstract

The complex composition of wine makes catechin determination via direct voltammetry challenging. In this study, we present an ex-situ voltammetric method using bare and modified carbon paste electrodes (CPE) to accurately determine catechin levels in wines. This method involves two steps: (a) extraction/adsorption onto the carbon paste, and (b) differential pulse voltammetry (DPV) measurement. Nanomaterial modifications of the CPE significantly improved selectivity in catechin extraction and quantification, offering a reliable approach for classifying and certifying Albanian and imported wines based on antioxidant content.

We successfully demonstrated this method using various CPE modifiers, including zeolite type X, Prrenjasi clay, single-walled (SWCNT), and multi-walled carbon nanotubes (MWCNT). The MWCNT-modified electrode exhibited the highest sensitivity, with a limit of detection (LOD) of 197 nM and a limit of quantification (LOQ) of 596 nM. Catechin concentrations in Albanian wine samples ranged from 665 to 2235 mg/L, with red wines showing higher levels than white wines.

A comparison using the Prussian blue spectrophotometric method confirmed these findings, showing consistent trends in increasing antioxidant content across both methods. The study highlights how environmental factors, such as soil composition, sunlight, and climate, influence catechin synthesis, with wines from warmer regions of Albania showing higher antioxidant levels. This method offers a valuable tool for ensuring the quality and classification of wines based on their catechin content.



# Electrochemical Determination of Uric Acid by Halloysite Nanotube Modified Electrode

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Halloysite nanotubes (HNTs), known as a naturally occurring hollow tubular aluminosilicate, have high surface area and cytocompatibility, making them a highly valuable materials [1]. Due to their environmental friendliness, wide availability in large quantities, and relatively low cost, halloysite nanotubes are increasingly being applied in the medical, food, and environmental sectors including development of biosensors [2,3,4]. Uric acid (UA) in abnormal concentrations in the body can result in various diseases such as hyperuricemia, gout, or Lesch-Nyhan syndrome, as well as heart-related diseases. Conversely, abnormally low levels of uric acid may contribute to the development of multiple sclerosis. Therefore, detecting uric acid concentration is crucial for diagnostic purposes [5]. The known concentration range of uric acid in serum is 0.13–0.46 mM [5]. In this study, HNT-modified pencil graphite electrode (HNT-PGE) was firstly developed, and the HNT modified electrode's surface was characterized based on SEM and electrochemical techniques. The voltammetric determination of uric acid was then performed and the limit of detection (LOD) was calculated. The effect of potential interferences upon to electrode response was also tested.

**Acknowledgement:** Arzum Erdem Gürsan would like to express her gratitude to the Turkish Academy of Sciences (TUBA) as a Principal member for its partial support.

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# A Graphene Oxide-Based Electrochemical Biosensor for the Detection of Pathogenic Microorganisms

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## Abstract

Pathogenic microorganisms are the causative agents that cause various infectious diseases and even death worldwide. Pathogens refer to including bacteria, viruses, fungi and parasites. Despite the victories gained with developed vaccines and antibiotics, new and multidrug-resistant pathogens constantly emerge [1,2]. They cause deaths worldwide by infecting their hosts through various means, especially through food, water and air. Bacteria such as *Escherichia coli* and *Staphylococcus aureus* as well as viruses such as *influenza* and *norovirus* are among the most common pathogens [3]. The early diagnosis of pathogenic microorganisms that cause infectious diseases is essential. Electrochemical biosensors, with their improved specificity, sensitivity, label-free nature, and cost-effectiveness, hold great promise for the rapid detection of various diseases. Nanomaterials provide great impact in the development of biosensing platforms such as high surface area, high electrical conductivity, biocompatibility, high sensitivity and selectivity [4]. Graphene oxide (GO), is a two-dimensional (2D) graphene derivative containing oxygen functional groups on its surface. It has become the basis of many advanced biosensors due to its extraordinary properties such as a high surface area, being biocompatible, having a stable structure, and electrical conductivity [5].

In this study, a novel label-free electrochemical genosensor was developed for the detection of pathogenic microorganisms using graphene oxide-modified disposable graphite electrodes (GO-PGEs). *Escherichia coli* (*E. coli*) bacteria was used as a model microorganism. The hybridization of complementary and non-complementary sequences to *E. coli* DNA probe immobilized to GO-PGE was monitored using electrochemical impedance spectroscopy (EIS) technique. The nanogenosensor was optimized for higher specificity and sensitivity. The optimized nanogenosensor successfully detected the PCR real samples. The designed nanogenosensor was submit the high selectivity and sensitivity for the diagnosis of pathogenic microorganisms. This platform can be extended further to develop biosensors for the detection of various other pathogenic microorganisms or microbiological diseases.

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# An Indirect Electrochemical Detection Of Creatinine In Urine Samples Using A Boron-Doped Diamond Electrode

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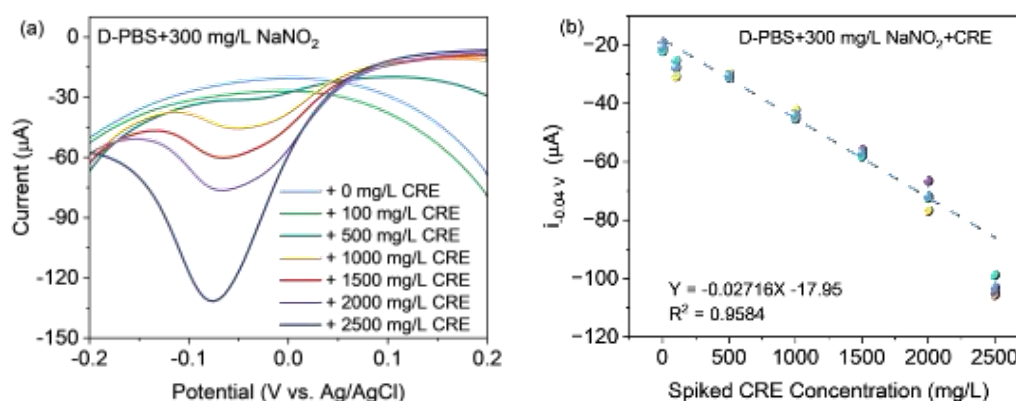
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Creatinine (CRE) is a metabolite from creatine and phosphocreatine and is generated through energy consumption in the muscle and tissue, which is filtered by the kidneys from blood into urine [1]. The CRE level in biological fluids, such as serum and urine, is a significant indicator of the body's renal functions and is vital in evaluating the body's hydration level, thyroidal malfunction, and muscular disorders [2]. Therefore, determining CRE in biofluids could provide related information about those functional processes, contributing to the health management and early diagnosis of acute diseases. Unlike blood, urine collection, handling, and disposal are simpler and more accessible, which is friendly to the long-term and frequent point-of-care testing and health monitoring with no disturbance to patient integrity. Boron doped diamond (BDD) electrode has been recognized as a kind of promising electrode material due to its wide potential window, low background current, excellent resistance to non-specific adsorption, and good stability [3], which is suitable for long-term electrochemical analysis in complex biofluids. In this work, the CRE in human urine was electrochemically determined indirectly by reacting with  $\text{NaNO}_2$  on a bare BDD electrode. First, gradient concentrations of CRE from 100 – 2500 mg/L (approximately 0.88 – 22 mM) were determined in buffer solution with the addition of  $\text{NaNO}_2$  (Fig.1 (a)). The linear relationship between reduction current and CRE concentration illustrated the possibility of creatinine determination by BDD (Fig.1 (b)). The Limit of detection of CRE in buffer solution is 178.7 mg/L (1.6 mM), which is lower than the healthy level of CRE in human urine (4.4 – 18 mM [4]). The spiked CRE in diluted urine samples determined by our method were compared with that from UV-Vis spectra based on the Jaffé method. The results showed a good agreement between both methods.

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## Figures



**Figure 1:** (a) Differential pulse voltammetry of 0-2500 mg/L CRE in D-PBS (Dulbecco's Phosphate Buffered Saline, pH=6.4) with addition of 300 mg/L  $\text{NaNO}_2$ . (b) The plot of reduction current at -0.04 V (vs. Ag/AgCl) with each CRE concentration.

# Thermophysical properties of Bromohexane + ethanol in a temperature region and local atmospheric pressure

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## Abstract

Knowledge of physical properties of liquid mixtures is essential for the understanding of molecular interactions existing between various species in a mixture, and thus the experimental determination of physical properties at different temperatures covering the whole composition range is almost a necessity from both theoretical and practical point of view. In this work we report the densities, sound speeds, and related thermodynamic excess properties, namely excess molar volumes and excess isentropic compressibilities, measured at temperatures from 283.15 K to 333.15 K under atmospheric pressure conditions for binary mixtures of 1-bromohexane + ethanol. The densities and sound speeds are measured using the density and sound speed analyzer DSA5000M by Anton Paar. Redlich-Kister polynomial is used to correlate the thermodynamic excess properties to test the quality of experimental data. Excess properties give insights into the molecular interactions between involved molecules and the peculiarities of their packing in the mixture. This research contributes to the thermodynamic database for the studied systems, offering essential novel data for validating and refining predictive models and equations of state.

*Keywords: density, sound speed, binary mixtures, bromohexane, temperature*

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# Electrochemical determination of lead by laser -scripted reduced graphene oxide electrode decorated with gold nanoparticles

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Over the past decade, surface water sources have been continuously polluted by harmful chemical substances, biological waste, and other contaminants, primarily due to rapid industrialization and human activities.[1] Among them, heavy-metal ions(HMIs) are a huge threat as they are very toxic, easy to accumulate, and non-degradable in the environment. The presence of lead ions ( $Pb^{2+}$ ) is associated with adverse effects on children's behavior, physical growth, cognitive skills, and educational achievement. [2] In this study, we present a graphene-based sensor for the detection of  $Pb^{2+}$  in water. The sensor utilizes a conductive film composed of reduced graphene oxide (rGO) incorporated with gold nanoparticles (AuNPs), fabricated through a one-step,  $CO_2$  laser-assisted co-reduction process. This method simultaneously reduces graphene oxide and gold cations to form the rGO@Au nanocomposite [3] Electrochemical characterization of –rGO@Au sensor was accomplished via Cyclic Voltammetry and Square wave anodic stripping voltammetry. [4] The sensor exhibited a sensitivity of 0.3367  $\mu A/ppb$ , a 5-30 ppb linear range, and a correlation coefficient of 0.9941.

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# EXTRACTION OF OILS FROM BIO WASTE BY DEEP EUTECTIC SOLVENTS

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Deep eutectic solvents (DES) have many outstanding features as they are easy to prepare, inexpensive, low-toxic, low volatile, and biodegradable, which make them increasingly attractive in industrial chemistry and green chemistry [1-4].

In this study the extraction of oils from sour cherry and apricot kernels were carried out using deep eutectic solvents in comparison with Soxhlet as conventional extraction method. Various deep eutectic solvents were synthesized consisting of choline chloride with urea, glucose, ethylene glycol and glycerol.

The extractions were performed in seed: solvent: DES ratio (1:6:1) which resulted in significantly increasing the oil yield. Soxhlet extraction with ethanol from apricot kernels resulted in 32.06% oil yield, while the extraction with choline chloride:glycerol (1:2) resulted in 57.99% oil yield. Application of DESs as novel co-solvent with organic solvents in comparison with the conventional method showed advantage also in reducing the energy (80°C vs 50°C), time (2h vs 3h) and solvent (150ml vs 30 ml) consumption.

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# Development of a DNA-based Electrochemical Biosensor for Rapid Thrombin Detection Using Nanostructured Gold Electrodes

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Early diagnosis of hemostatic disorders, such as thrombosis and hemophilia, relies on the rapid and accurate detection of biomarkers like thrombin. [1] Electrochemical biosensors, capable of converting biomolecular interactions into electrical signals, are powerful tools for detecting biomarkers. Their high sensitivity and specificity enable precise quantification, facilitating early diagnosis of blood coagulation imbalances and effective treatment monitoring. [2,3] In this work, we developed an electrochemical biosensor for the precise quantification of thrombin in biological samples. The sensing platform is based on nanostructured gold electrodes, fabricated using a combination of inkjet printing [4] and click-sintering techniques, [5] resulting in a high surface area and optimized electrochemical properties. This nanostructuration significantly increases the sensor's sensitivity, enabling the detection of ultra-low concentrations. Here, we propose as biorecognition element a thrombin structure-switching aptamer, modified with one extremity with a redox tag, and presenting a portion that is displaced only in the presence of the target. When the target is present, the displaced portion can bind a capture sequence immobilized on the electrode, giving a current signal. This current is directly proportional to the thrombin concentration in the sample. [6] Ongoing research aimed at optimizing experimental conditions will further enhance the biosensor's performance, making it a valuable tool for early disease detection. This analytical platform has the potential to be applied in various fields, such as clinical diagnosis, monitoring of anticoagulant therapies, and biomedical research.

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# Electrochemical response of senecionine at carbon-based electrodes using carboxyl graphene as a surface modifier

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Senecionine, one of the many identified toxic pyrrolizidine alkaloids, is dangerous for humans due to its hepatotoxic, carcinogenic, and genotoxic effects. Chromatographic methods are widely used to detect and quantify these toxins in herbal preparations. The referent method, described in European pharmacopeia, is based on HPLC MS-MS. Based on the literature research, up to date, there are no studies on the electrochemical behavior of senecionine. In this work, we have studied the electrochemical behavior of senecionine using carbon-based electrodes such as solid glassy carbon electrodes, screen-printed carbon electrodes and boron-doped diamond electrodes. Carboxylic graphene and its nanocomposite were applied as a surface modifier. Cyclic voltammetry (CV) and differential pulse voltammetry (DPV) techniques were applied to observe the electrochemical behavior of senecionine on each electrode. Experimental parameters (supporting electrolyte, scan rate, potential range, and modifier concentration) were optimized to enhance sensor performance. Phosphate buffer (pH 7.4) and KCl/NaOH (pH 10) were used as a supporting electrolyte. The best results for the sensitivity and repeatability of the response to senecionine were obtained using carbon screen-printed electrodes, modified with carboxyl graphene (GCOO). The type of the electrode and modifier has a high impact on the sensor's function, sensitivity and selectivity. Further work is necessary to investigate the other factors that affect the interaction of the analyte with the electrode and validate the method's application in complex sample matrices with herbal ingredients.

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# Detection of Cellular Stress Biomarkers Using Plasmonic Sensors with Potential Application in Organ-on-a-Chip Platforms

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## Abstract

Plasmonics provides a powerful toolbox for sensitive and label-free detection of biomolecules[1]. In this study, a plasmonic sensor is pursued for the detection of Matrix Metalloproteinase-3 (MMP3), a key cellular stress biomarker and a crucial indicator in the diagnosis of diseases such as rheumatoid arthritis [2,3,4]. MMP3 plays a significant role in extracellular matrix remodeling and inflammation, making its accurate and sensitive detection essential for both cell stress response and arthritis diagnosis.

We characterized a sandwich assay format for MMP3 detection using surface plasmon resonance biosensor with the gold sensor surface coated with a thiol self-assembled monolayer for covalent coupling of anti-MMP3 capture antibody. After introducing MMP3-containing samples to the sensor surface, a detection antibody specific to a different epitope of MMP3 was added and specificity in the analysis of cell-culture medium is evaluated.

A dedicated optical setup will enable sensitive and specific real-time analysis of MMP3 detection by using a miniature sensor elements through surface plasmon-enhanced fluorescence when integrated into organ-on-chip platforms. This tool will serve for detecting biomarkers related to cell stress studies in tendon-on-chip applications. This approach will offer label-free continuous protein detection with spatial interrogation. In the future, its incorporation into broader biosensing platforms could set a new standard in clinical diagnostics and precision medicine.

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## Acknowledgements

This work was supported by the Czech Science Fund, project SOMICELL (23-05908K).

# Investigating the impact of open burn pits on air pollution in Albania

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## Abstract

Limited air quality studies carried out in Tirana over the last decades indicate that PM<sub>10</sub> and PM<sub>2.5</sub> levels frequently exceed the EU limit and WHO guidelines [1-3]. In addition to PM emissions, primary and secondary air pollutants contribute to formation of complex gaseous toxic mixtures of CO, NO<sub>x</sub>, SO<sub>2</sub>, O<sub>3</sub> and volatile organic compounds (VOCs), and other poorly characterized pollutants that can lead to a range of adverse health effects, including development of lung cancers, asthma and chronic obstructive pulmonary diseases, respiratory infections, cardiovascular diseases, neurological disorders and stroke [4,5]. Open pit burning of mixed municipal waste can generate highly toxic mixtures of gaseous and PM pollutants, including dioxins, furans, heavy metals, PAHs, CO, SO<sub>2</sub>, NO<sub>x</sub>, and environmentally persistent free radicals. This collaborative research project- funded through the READ (Research Expertise from the Academic Diaspora) program - aims to determine the airborne concentration and chemical composition of PM pollution in Tirana and adjacent areas with active and frequent open burn pits. A TECORA ECHO PM<sub>10</sub>/PM<sub>2.5</sub> Sampler is being used for PM measurements in 4 representative stations for at least 2-week intervals capturing spatial and seasonal variations in airborne PM<sub>2.5</sub> and PM<sub>10</sub>. Gravimetric analysis will be complemented with chemical composition analysis, including for heavy metals, PAHs, free radical (ROS) generation, dioxins and other organic and inorganic compounds, will be carried out at UMASS Lowell, by using a range of modern techniques. Deposition of dust fall by the gravimetric standard method (ASTM 2017, D1739 – 98) will be measured at the same stations to expand the coverage time and further chemical composition analysis will be carried out, intending to identify signature pollutants associated with open burning of waste streams, including plastics, batteries, electronics, or medical waste. The obtained results can serve as the first critical step in understanding the air pollution toxicology, their sources and health impact, and can inform larger scale monitoring efforts.

*Acknowledgment: This work is funded by Research Expertise from the Academic Diaspora Fellowship (READ) program.*

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**Figure 1:** TECORA ECHO PM<sub>10</sub>/PM<sub>2.5</sub> Sampler nearby “Vasil Shanto” crossroad

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## Nanobiotics Development: Utilizing Natural Resources to Improve Therapeutic Efficacy

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Antibiotic resistance presents a significant challenge in the search for new therapeutic agents, making the development of effective alternatives essential. This presentation focuses on using natural compounds to enhance therapeutic efficacy, with a particular examining tropolone, betha-thujaplicin, carvacrol, thymol, and chlorothymol.

Tropolone and betha-thujaplicin, derived from natural sources, exhibit significant antioxidant and potential but faces challenges such as low solubility and thermal instability. Similarly, carvacrol and thymol, both found in thyme oil, possess antibacterial properties; however, their low bioavailability and volatility pose a challenge.

To address these limitations, lipid-based nanocarriers utilizing high-pressure homogenization techniques were prepared. Comprehensive characterization including particle size, zeta potential, and encapsulation efficiency indicated that these nanocarriers exhibited higher encapsulation efficiency and stability. Our study further investigated the antimicrobial activity of these nanobiotics against clinically isolated microorganisms, revealing significant differences in antimicrobial efficacy among the bioactive compounds. These compounds showed potential against antibiotic-resistant strains, highlighting their role as alternative therapeutic agents in an era of increasing antibiotic resistance.

This work highlights the potential of utilizing natural resources to develop novel nanobiotic treatment that can effectively address various health challenges, particularly in resistant microbial infections.

**Keywords:** nanoemulsions, nanostructured lipid carriers, antimicrobial, thymol, chlorothymol, carvacrol, tropolone, betha-thujaplicin

\*Mimoza Basholli Salihu and Aida Loshaj Shala contributed equally.

Mimoza Basholli-Salihu, Aida Loshaj-Shala, Toskë Kryeziu are members of the NANOALB research group.

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# Characterization with molecular spectroscopy of 3-[2-(thiazol-2-yl)hydrazinylidene]chroman-2,4-dione

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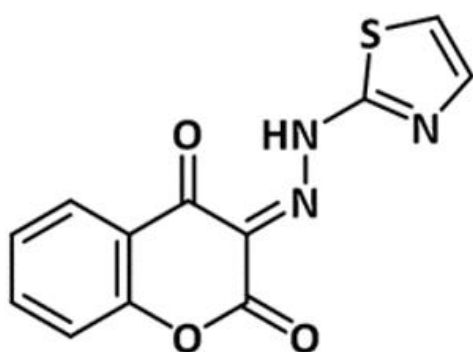
## Abstract

In this study, spectroscopic methods were used to analyze the new derivative of coumarin - 3-[2-(thiazol-2-yl)hydrazinylidene]chroman-2,4-dione with a complex organic structure through UV-Vis and IR spectroscopy. UV-Vis measurements were conducted under different pH conditions, ranging from pH=1-12, to observe the impact of pH on the electronic behavior and structure of the substance. In the UV-Vis spectra, a significant shift was observed in the first band (212 nm) in a highly acidic environment (pH=1), suggesting the protonation of the substance. Additionally,  $\pi - \pi^*$  (190-210 nm) and  $n - \sigma^*$  (250 nm) electronic transitions related to the substance's structure were identified, focusing on the free electron pairs of heteroatoms such as oxygen and nitrogen. Through the changes in pH, spectral shifts and structural alterations were observed, particularly in basic pH where coumarin structure breakdown and regeneration occurred. In IR spectroscopy, the characteristic vibrations of functional groups such as the OH group ( $3650-3450\text{ cm}^{-1}$ ), aromatic CH groups ( $3100-3050\text{ cm}^{-1}$ ), and the keto group ( $1750\text{ cm}^{-1}$ ) were analyzed. Additionally, benzene deformations and the presence of diazo group (N=N) were observed in the infrared spectrum. This combination of methods helped identify the characteristic groups and determine the structure of the substance, demonstrating the connection between its structure and behavior under different pH conditions.

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## Figures



**Figure 1.** Derivative of coumarin 3-[2-(thiazol-2-yl)hydrazinylidene]chroman-2,4-dione.





# Impact of Protonation on the Adsorption Properties of Phenols on Graphene Oxide: Insights from DFT Calculations

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With the rapid advancement of industrialization, a wide array of carbon-based and inorganic materials is increasingly used in essential sectors such as petrochemicals, textile dyeing, coal industry, polymer production, biopharmaceuticals, and process engineering. These manufacturing processes frequently result in the generation of polluted water, containing complex constituents—such as heavy metals, dyes, pesticides, phenolic compounds . . . —that are often non-degradable or challenging to break down, posing significant risks to toxicity and environmental health. Phenolic compounds are often overlooked, yet their discharge can severely harm aquatic life, soil, and overall ecosystems, posing risks to health. Currently, various methods—such as organic carbon adsorption, advanced oxidation processes, membrane-based techniques, and reverse osmosis—are employed to remove carbon-based contaminants from polluted water. However, the stability of phenolic pollutants presents significant challenges, making these decomposition methods not only lengthy and costly but also prone to by-product formation. In recent decades, adsorption treatment has emerged as a preferred approach due to its operational simplicity and cost-effectiveness. Among the various adsorption strategies, the use of nanomaterials, particularly graphene oxide (GO), has gained significant attention for its effectiveness in pollutant removal [2]. Graphene oxide is a versatile nanomaterial known for its high surface area, abundant functional groups, and remarkable adsorption properties. These characteristics enable GO to effectively capture a wide range of contaminants, including phenolic compounds, thereby providing a promising solution for water treatment applications. In addition to experimental methods, computational simulation techniques are utilized to investigate and clarify the entire reaction process at the molecular level. In this study, we systematically explore the interactions between various phenolic compounds commonly present in wastewater, including phenol, 2,4-dichlorophenol, p-cresol, pentachlorophenol, 4-(2,4-dimethylheptan-3-yl)phenol, 4-nitrophenol, bisphenol A, and 2-chlorophenol, and their adhesion to graphene oxide. Our primary objective is to analyze the variations in adsorption energy, adsorption distance, and electron density distribution when neutral or protonated phenolic compounds interact with graphene oxide, utilizing first-principles calculations. Additionally, Reduced Density Gradient (RDG) analysis enables us to examine both strong and weak van der Waals interactions—both repulsive and attractive—between phenolic compounds and the graphene oxide surface. This comprehensive analysis allows us to assess distinct adsorption behaviours effectively. The findings of this research indicate a promising strategy for the removal of phenolic pollutants from wastewater.

\*[The results presented here are part of the study conducted under the Bilateral Kosovo-Albania Project, titled 'Treatment of Wastewater Contaminated with Phenols Using 2D Carbon Nanomaterials (Graphene and Graphene Oxide) as Adsorbents: An Experimental and Theoretical Study]

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# Determination of 5-hydroxymethylfurfural using molecularly imprinted polymer in combination with carboxylic graphene-Ni nanocomposite

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## Abstract

Maintaining controlled levels of 5-hydroxymethylfurfural (5-HMF) is crucial for overall health, due to its potential toxicity and its association with various diseases. In order to determine the concentration of this furanic compound we present a sensor based on a molecularly imprinted polymer functioning as a receptor, converting chemical interactions into electrical signals on a screen-printed electrode (SPC). The screen-printed electrodes were modified with carboxylic graphene-Ni nanocomposite. Graphene provides electrical conductivity, which is essential for efficient charge transfer in electrochemical sensors, while its high surface area increases the interaction with the analyte, which leads to higher sensitivity. Due to their catalytic properties to further enhance the electrochemical response, nickel ions were incorporated in carboxylic graphene. The molecularly imprinted polymer was prepared using methacrylic acid as a monomer, divinylbenzene as a crosslinker and azobisisobutyronitrile (AIBN) as an initiator in the presence of 5-hydroxymethylfurfural as the template molecule that impregnates the polymer. The sensor's properties and response were analyzed using cyclic voltammetry (CV), differential pulse voltammetry (DPV), and electrochemical impedance spectroscopy (EIS). The electrochemical sensor exhibits a linear range for concentration range from 0.1 to 5 mM.

**Key words:** 5-hydroxymethyl-2-furfural, cyclic voltammetry, honey, carbon paste electrode.

**Acknowledgments:** We thank the Albanian Academy of Sciences for financial support.

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# In Vitro Evaluation of Cytotoxicity Induced by Particulate Matter in Human Lung Epithelial Cells (A549)

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**Background:** Particulate matter (PM), especially PM<sub>2.5</sub>, is a contributor to respiratory diseases, as it can infiltrate the lungs and trigger inflammation.<sup>1,2</sup> A549 cells, a model for human alveolar epithelial cells, are susceptible to PM-induced damage, which can result in impaired lung function. Investigating the cellular responses of A549 cells to PM exposure is essential for understanding the full scope of air pollution's detrimental effects on lung health.<sup>3,4</sup>

**Aims:** This study aims to evaluate the cytotoxic impact of PM<sub>2.5</sub> on A549 lung epithelial cells sourced from two urban areas in Kosovo: Prishtina and Obiliq. We aimed to assess the dose- and time-dependent effects of PM<sub>2.5</sub> on cell viability and to provide insights into how PM exposure compromises lung health.

**Methods:** A549 cells were cultured and exposed to varying concentrations of PM<sub>2.5</sub> (25, 50, 70, and 100 µg/ml) for 24 hours. MTT assays were used to determine cell viability and metabolic activity after exposure, reflecting the cytotoxic effects of PM<sub>2.5</sub> on the cells.

**Results:** A dose-dependent decline in cell viability was observed in A549 cells, with higher concentrations of PM<sub>2.5</sub> leading to a more pronounced reduction in cellular metabolic activity and increased cytotoxicity after 24 hours of exposure.

**Conclusions:** This study highlights the dose-dependent toxic effects of PM<sub>2.5</sub> on human alveolar epithelial cells, underscoring the damaging impact of air pollution on respiratory health. These findings contribute to a growing understanding of the potential risks posed by PM<sub>2.5</sub> exposure, particularly in relation to the development of respiratory diseases.

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# **Unlocking the Anti-Cancer Potential of Quercetin: Strategies for Nanotechnology in Encapsulation**

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Cancer remains a leading cause of mortality worldwide, with conventional therapies like chemotherapy facing significant challenges, such as drug resistance and non-specific targeting. Quercetin (QUE), a naturally occurring flavonoid, has garnered attention for its potential in cancer therapy, primarily due to its antioxidant properties and ability to modulate various cancer-related pathways. Despite this, its clinical application is limited by poor solubility and low bioavailability.

Nanotechnology-based encapsulation strategies have emerged as a promising approach to overcome these limitations, offering enhanced delivery and efficacy of quercetin in cancer treatment. Various nanoformulations, including liposomes, polymeric micelles, and inorganic nanoparticles, are being explored to improve quercetin's solubility, stability, and targeted delivery. These systems hold the potential to optimize quercetin's therapeutic effects by enabling better interaction with cancer cells while reducing side effects commonly associated with free quercetin.

By employing advanced nanocarrier systems, encapsulated quercetin can achieve more precise targeting of cancer cells, thereby enhancing its therapeutic potential as a novel anti-cancer agent in modern therapeutic approaches.

# Reduced graphene oxide decorated with Fe<sub>2</sub>O<sub>3</sub> nanoparticles composite carbon paste electrode (CPE) for voltammetric determination of atenolol

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## Abstract

An effective electrochemical sensing platform for the determination of atenolol (ATN) based upon magnetic nanoparticles Fe<sub>2</sub>O<sub>3</sub>/reduced graphene oxide (rGO) bulk modified carbon paste electrodes (Fe<sub>2</sub>O<sub>3</sub>-rGO/CPE) is reported. The electrochemical studies and measurements were carried out by using voltammetry (CV) and square wave voltammetry (SWV) techniques. The nanocomposite-modified carbon paste electrode (Fe<sub>2</sub>O<sub>3</sub>-rGO/CPE) exhibited enhanced electrocatalytic performance for the determination of ATN. The proposed method using Fe<sub>2</sub>O<sub>3</sub>-rGO/CPE sensor is characterized by high sensitivity of measurements, with the linearity of ATN in the range from 40 to 3138  $\mu\text{mol L}^{-1}$ . The lowest detection limit achieved on the Fe<sub>2</sub>O<sub>3</sub>-rGO/CPE nanocomposite electrode for 10 s of preconcentration time was 58  $\mu\text{mol L}^{-1}$  ATN in 0.1 mol L<sup>-1</sup> H<sub>2</sub>SO<sub>4</sub> of pH 2.0 using square wave technique. The nanommodified Fe<sub>2</sub>O<sub>3</sub>-rGO/CPE sensors showed a good reproducibility and repeatability (RSD  $\leq$  5%,) for ATN determination. The reduced graphene oxide decorated with magnetic nanoparticles Fe<sub>2</sub>O<sub>3</sub>-rGO results with a good enhancement in the sensitivity of the sensor through a combination of increased surface area and improved electron transfer kinetics. Finally, the fabricated Fe<sub>2</sub>O<sub>3</sub>-rGO/CPE exhibits high sensitivity and good stability towards the sensing ANT and has the potential to be utilized as a clinical assay and quality assurance (QA) in pharmaceutical products.

**Keywords:** Atenolol, reduced graphene oxide, nanocomposite, modified glassy carbon electrode, square wave pulse voltammetry.

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## Figures



**Figure 1:** Schematic determination of ATN with Fe<sub>2</sub>O<sub>3</sub>-rGO/CPE sensor





# Occurrence of microplastics in fishes from aquatic ecosystems of northern Kosovo

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## Abstract

This study aimed to assess the possible presence of environment contaminant microplastics (MP) in the digestive systems of fish samples captured in the northern region of Kosovo as well as in the corresponding surface waters. Given that fish are consumed by residents, they may represent a potential source of microplastics for humans. The identification of MP was attempted within specimens isolated from *Squalius cephalus*, *Rutilus rutilus*, *Chondrostoma nasus*, *Alburnus alburnus*, *Alburnoides bipunctatus*, and *Lepomis gibbosus*. The MP analysis consisted of two steps, i.e. preliminary evaluation by optical microscopy followed by tentative chemical characterization by Fourier-transform mid-infrared attenuated total reflection spectroscopy (ATR-FTIR) for the investigation of plastics polymers [1]. The results, indicating that microplastics were present in all studied fish species, were in accordance with other studies showing that MP items enter the trophic chain with a potential impact on food security and human health [2]. Information from the statistical evaluation of the spectroscopic data is also presented.

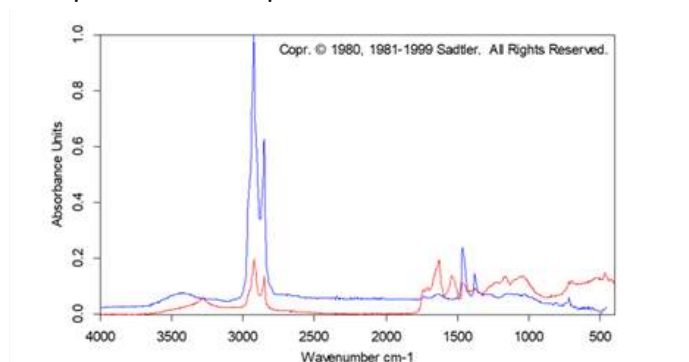


Figure 1. Identification of polyethylene in a fish sample of the presented study

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## Per- and polyfluoroalkyl (PFAS) contamination of irrigation waters in Albania

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### Abstract

This research project focuses on investigating per- and polyfluoroalkyl substances (PFAS) contamination of surface and underground water used for irrigation in Albania. The work was funded by the *Research Expertise from the Academic Diaspora Fellowship (READ) program*. We collected water samples (n=93) in regions locations across the country that targeted: a) surface water irrigation sites (e.g. rivers, streams and reservoirs); b) ground water systems (e.g. wells) and c) waterbodies near industrial sites that could potentially use PFAS. Samples were analyzed with liquid chromatography tandem-mass spectrometry (LC-MS/MS). In cooperation with groups that produce nanosensors, PFAS analyzes are being experimented with, so far we have no validated results. From the target list of 47 target PFAS compounds we detected 17 compounds. The highest % detection correspond to PFPrA (C3) at 100% and PFPxH (C6) and 55% all samples. Total PFAS concentrations were the highest in hospital wastewater samples (total PFAS =  $2.2 \cdot 10^6$  ppt) and a natural gas distribution line ( $2,5 \cdot 10^3$  ppt). Irrigation wasters highest levels were measured in Benja Lake (439 ppt) and two wells in Tirane (283 ppt) and Kucove (307 ppt). Overall, the high levels of PFAS in hospital waste and industrial sources was driven mostly by the ultra-short chain PFAS that are less persistent in the environment compared to the long chain PFAS. The most concerning long chain PFOA and PFOS were detectable at small levels only in a few samples. Although these results are good news, they should be interpreted with caution given that this study's samples may not represent every possible emission scenario. This pilot project strengthens Albania's research infrastructure, contributing to future water quality management strategies aimed at mitigating the impacts of industrial and agricultural pollution on human health.

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# Primary Results from Nanopore and Next-Generation Sequencing of Tomato Samples in Albania

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## Abstract

This research study investigates the role of Oxford Nanopore technologies in detecting and characterizing viruses, mainly the Tomato Brown Rugose Fruit Virus (ToBRFV) in tomato plants grown in greenhouses in Albania. The work was funded by the National Agency for Science Research and Innovation in Albania (NASRI), through NanoAlb.

ToBRFV in Albania was reported for the first time in 2022 [1] and from this period there has been a significant spread which should be studied quickly and accurately.

The period for sampling was based on the characteristics of the tomato vegetation cycle and the development of ToBRFV, it was in greenhouses (September - October - November 2023). During the sampling, we aimed to carry out a selection of plants that showed spotting, mosaic and narrowing of the upper leaf blades [2].

According to the manufacturer's instructions, the nanopore sequencing experiment was conducted using the cDNA-PCR sequencing kit V14 (SQK-PCS114). The initial sample consisted of 500 ng of total RNA extracted from symptomatic tomato plants in Albania. The first run of Oxford Nanopore sequencing yielded 11.04k paired-end reads, which were reduced to 8.78k after quality filtering and clean-up. High-quality reads were de novo assembled using Geneious software, resulting in 2,500 contigs with lengths ranging from 40 to 22,400 nucleotides. A reference mapping against the Tomato Brown Rugose Fruit Virus (ToBRFV) sequence from GenBank revealed an 84% genome coverage, with 8 reads matching this virus. The read lengths varied from 120 to 860 nucleotides.

For comparison, next-generation sequencing (NGS) was performed on the total RNA from the same tomato sample, generating approximately 55 million paired-end reads. After the quality filtering process, the number of high-quality reads decreased to 2 million. These reads were also de novo assembled, producing 35,334 contigs, with lengths ranging from 50 to 57,863 nucleotides. A reference mapping against the ToBRFV genome retrieved from GenBank provided 100% coverage, with 34 contigs confirmed through a BlastX search via Geneious software [3]. The lengths of these contigs ranged from 50 to 4,800 nucleotides.

These results demonstrate the efficacy of Oxford Nanopore Technologies (ONT) for rapid detection and partial genome characterization, despite lower read depth and coverage compared to NGS. The study underscores the potential for using Nanopore sequencing in resource-limited settings, while highlighting the robustness of NGS for comprehensive viral genome analysis.

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# Synthesis, characterization, and electrocatalytic properties of $\text{SmMn}_{0.5}\text{M}_{0.5}\text{O}_3$ ( $\text{M} = \text{Cr, Fe, Co, Ni}$ ) perovskite materials

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In recent decades, significant research has focused on perovskite-type compounds ( $\text{ABX}_3$ ), making them one of the most thoroughly studied material classes. The growing scientific interest in these compounds is due to their flexible composition and structure, which results in a wide variety of remarkable and unique properties. Of particular interest are oxide perovskites with manganese at the B-site and certain lanthanides at the A-site, as they offer both scientifically and practically intriguing properties. This study focuses on the synthesis and characterization of novel complex perovskites with the formula  $\text{SmMn}_{0.5}\text{M}_{0.5}\text{O}_3$ , where M can be Cr, Fe, Co, or Ni. The assumption that compounds with this composition would have a perovskite structure was confirmed by calculating the tolerance factor. These compounds were synthesized by the Solution combustion method using glycine as fuel. The perovskites obtained were characterized by X-ray powder diffraction (XRPD), scanning electron microscopy (SEM) with energy dispersive X-ray spectroscopy (EDX), infrared spectroscopy (IR) and cyclic voltammetry. The XRPD patterns confirmed the compounds purity and showed that all the materials in the series share the same structure. SEM images revealed a porous morphology characteristic of perovskites obtained by the solution-combustion method, and EDX analysis verified the 2:1:1 ratio of Sm:Mn:M. IR spectroscopy further examined the perovskites, with spectra in the far-IR region displaying characteristic bands from the stretching and bending vibrations of Mn/M–O and Sm–O bonds. The shifts in these bands due to different M cations matched theoretical predictions. Cyclic voltammetry, conducted using paraffin-impregnated graphite electrodes (PIGE) modified with the perovskites, confirmed their electrocatalytic activity, specifically for the oxidation of  $\text{OH}^-$  ions and  $\text{H}_2\text{O}_2$  in phosphate buffer solution.

# Application of factorial analysis for the design of a modified carbon-based sensor for the determination of azithromycin

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## Abstract

There are several types of antibiotics, natural and synthetic, which inhibit the growth of bacteria by inhibiting the growth of their cell wall. Azithromycin is one of them used to cures various diseases and its discovery marked a major turning point in infectious medicine. Although many lives have been saved, they have become unsuitable for some diseases over time. Drug-resistant bacteria grow and spread, and some even pass their resistance on to other bacteria.

Our aim in this work has been on the optimisation of an alternative electrochemical method for the determination of azithromycin as one of the most used antibiotics. There are several factors influencing simultaneously on the results of an analytical chemistry procedures. The methodology used by the most analysts to optimize an analytical procedure is the classical one, called univariate technique, which is time consuming and does not take into account the interaction between factors. In order to assess which kind of factors are important and to estimate the quantitative role of them and their interactions, factorial design is applied. Through factorial design it is possible to propose an empirical model that might provide a good description of the data. The methodology used in factorial design requires the formulation of a polynomial model approximating the relationship between measured signal (I-current in our case) and the factors ( $X_i$ ) taken into consideration. In our experiment we have examined three factors that influence the measured signal: the mass of the carbon paste modifier used, which is graphene oxide, dopped with Cu; the pH value of the buffer used as an indifferent electrolyte and the measurement time after each addition. The values found with the help of the models of the equations (coded and real variables) agree with the experimental values, which show that the found equations describes our experiment very well and consequently, they are adequate. From the found models it resulted that the most significant factor and interaction between factors are the pH of the buffer and the mass of modifier and pH together.

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# Graphene-Based Electrochemical Lateral Flow for Alzheimer's Disease Prognosis

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Alzheimer's Disease (AD) is the most common type of dementia [1], currently relies on diagnostic methods that are expensive, invasive, or time consuming. Blood biomarkers represent a significant step forward in addressing these challenges [2]; nevertheless, the lack of cost-effective, simple testing protocols remains a critical barrier.

Here, we propose a novel, cost-effective Point-of-Care (PoC) system designed for early AD diagnosis and monitoring disease progression. Leveraging a green, IR-laser-assisted low-cost print/stamp technology, we fabricate reduced graphene oxide (rGO) electrodes directly integrated into lateral flow assay (LFA) strips [3]. These rGO electrodes can be functionalized with aptamers that specifically bind to key AD biomarkers, enabling real-time monitoring of the disease. Binding events between the aptamers and target biomarkers induce detectable changes in the electrochemical signal, allowing for rapid, sensitive, and reliable detection.

This PoC system provides a promising, non-invasive approach to AD diagnostics, offering a streamlined, accessible solution for early detection and disease management.

## Acknowledgements

This work is part of the 2D-BioPAD project that has received funding from the European Union's Horizon Europe Research and Innovation Programme under grant agreement No. 101120706.

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# Nitrate concentration and human health risk assessment in different age groups of population

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## Abstract

A Human health risk assessment was proposed by United States Environmental Protection Agency (USEPA) such as hazard identification, dose response assessment, exposure assessment, and risk characterization [1, 2]. Estimation daily intake (EDI: mg/kg day) was computed to determine the doses of NO<sub>3</sub> - received through individual ingestion pathway. The drinking water pathway is computed by using EDI, which indicates the measure of chemical substance ingested through drinking per kilogram of body weight per day [3, 4]. Adopted methodology to assess the human health risk goes through these elements: **i.** Hazard identification [non-carcinogenic risk] **ii.** Dose response assessment [Oral intake - Rdf] **iii.** Exposure assessment [Chronic daily intake by drinking water] **iv.** Risk characterization in children, teenagers, adults – [Oral hazard quotient *evaluated* by Hazard Quotient HQ].

The results of the study indicated that the nitrate concentration in many brands of bottled water is lower than the standard limit, therefore, the consumption of bottled water does not create a threat to the health of consumers.

Based on risk assessment and data analysis, the highest value HQ was associated with the age group of children, thus the sensitivity should be applied to the selection of drinking water brands for this age group. The mean HQ values for nitrate in different groups of children, teenagers and adults were 0.3737, 0.2638 and 0.2114, respectively. The hazard quotient for the population consuming bottled water, appropriate strategies should be considered in order to reduce the concentration of nitrate in bottled water.

**Key words:** Nitrates levels, Bottled drinking water, Human health risk, IBA, FDA

Tab. 1 The statistical summary of EDI and HQ – values for different age groups

Age Groups	EDI - Daily nitrate consumption			HQ - the risk of non-carcinogenic substances		
	Children	Teenagers	Adults	Children	Teenagers	Adults
EDI & HQ						
Mean	0.35	0.10	0.07	0.30	0.09	0.06
Min	0.07	0.02	0.02	0.06	0.02	0.01
Max	1.05	0.32	0.22	0.91	0.27	0.19

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[https://nap.nationalacademies.org/login.php?record\\_id=11537#:~:text=The%20Essential%20Guide%20to%20Nutrient%20Requirements](https://nap.nationalacademies.org/login.php?record_id=11537#:~:text=The%20Essential%20Guide%20to%20Nutrient%20Requirements)

# Impact of Particulate Matter Exposure on Human Umbilical Vein Endothelial Cells: Insights into Oxidative Stress, Inflammation, and Endothelial Dysfunction

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This paper shows a literature review of the effects of PM<sub>2.5</sub> in Human umbilical vein endothelial cells (HUVEC). The purpose is a) to inform the reader about the up-to-date literature of the mechanisms by which PM particulates cause endothelial damage and b) to raise collective awareness on the effect of air pollution in the disease linked to the cardiovascular system. PM<sub>2.5</sub> presents a pollutant with a high potential of causing cardiovascular and pregnancy-linked complications, where the most common one is preeclampsia[1]. Results from *in-vitro* studies emphasize a connection between PM<sub>2.5</sub> concentration and their cytotoxic effect in endothelial cells [2]. HUVEC represents one of the most suitable *in vitro* models to analyze the changes in the endothelium post-exposed to the cytotoxic action of PM<sub>2.5</sub> due to the fact that a) they are cells of human origin, b) they are easy to isolate and culture, c) standard protocol for their cultivation eases experiment result reproduction d) they are cost-effective and e) they are the most commonly used cell cultures thus making the experiment results more understandable to the scientific community [3,4]. The consequences of short time (24,48,72hr) and long time (≥ two weeks) exposure show an elevation in pro-inflammatory proteins (e.g. IL-6 and TNF-α), elevation of oxidative stress markers, as well as emphasis on apoptosis through activation of the caspase-8 pathway [4]. The following table summarizes the important events of the action of PM<sub>2.5</sub> in HUVEC, based on the relevant field literature of the last ten years, highlighting the need of excessive research in this field.

**Acknowledgments:** We express our sincere gratitude for the funding provided by the European Commission under the project titled “Nanoparticles in Environment and Medical Research” (NanoKos - 438247).

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Study (Author, Year)	Inflammatory Markers	Oxidative Stress Markers	Apoptotic and Genotoxic Markers	Dosage	Exposure Duration	Health Outcome Studied	Experimental Model
Garcia et al. (2023)	TNF-α, IL-6	ROS	N/A	25 µg/m <sup>3</sup>	Chronic	Preeclampsia, endothelial dysfunction	HUVEC
Kim et al. (2022)	TNF-α	ROS	Caspase-8, p53, DNA damage	80 µg/m <sup>3</sup>	24 hours	Apoptosis, endothelial dysfunction	HUVEC
Wang et al. (2020)	N/A	ROS, SOD	N/A	100 µg/m <sup>3</sup>	72 hours	Endothelial barrier dysfunction	Endothelial cells
Scherzad et al. (2017)	TNF-α	ROS, MDA	DNA damage, γ-H2AX	15 µg/m <sup>3</sup>	48 hours	Oxidative stress, endothelial damage	HUVEC

**Figure 1:** Summary of PM<sub>2.5</sub> impact results in different *in vitro* models

# Advances and Perspectives in Near-Infrared Fluorescent Organic Probes for Surgical Oncology

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**Background:** Surgical oncology relies on precise imaging to detect and remove tumors. Near-Infrared (NIR) fluorescence imaging has become essential for this, offering high-resolution, real-time visualization during surgery. The light in NIR range of 700–1,700 nm is safe and does not harm patients as it penetrates deep tissues and has less autofluorescence readying the image for better clarity than the normal techniques. The use of NIR molecular probes in particular tumor-specific probes have led to advancement in cancer imaging due to the enhanced sensitivity and specificity. Many of the recently developed multifunctional NIR dyes target the tumour and also have other therapeutics design, which is aimed at amelioration of the surgical methodology and the way cancer is managed.

**Aims:** This review highlights recent advancements in NIR probes for surgical oncology, focusing on their design, applications, and future potential.

**Methods:** Probe Design: NIR organic probes were synthesized for tumor imaging using the NIR-II window, ensuring deep tissue penetration and high-resolution imaging. Nanoparticles and small-molecule dyes were conjugated with tumor-targeting ligands (e.g., peptides, antibodies) for specificity. Technological Innovations: Innovations included photostable, biocompatible NIR-II dyes with enhanced surface modifications to improve circulation and reduce toxicity. Pre-Clinical and Clinical Studies: Probes were tested in murine tumor models and clinical settings, demonstrating success in real-time tumor visualization, enhancing precision in tumor resection during surgery.

**Results:** NIR-II Probe Innovations: Recent advancements have led to the creation of probes with remarkable tissue penetration (over 5 mm depth) and high-resolution imaging. Novel organic molecules with optimized structures exhibit fluorescence in the NIR-II range (1000-1700 nm), allowing clear differentiation between cancerous and normal tissues. Comparative Performance: NIR-II probes, particularly the novel p-FE derivative, demonstrated a 3x higher signal-to-noise ratio (SNR) compared to traditional NIR-I dyes, enabling accurate tumor margins in surgical settings. In contrast to conventional fluorescence techniques, the enhanced contrast in deep tissues reduced the false positive rates in preclinical models by 20%. Imaging Results: In murine models, NIR-II probes significantly improved tumor resection accuracy, with a 95% detection rate of micro-tumors (<0.5 mm). Imaging results from clinical trials further supported the potential of these probes, highlighting a 40% improvement in visual clarity during cancer surgeries.

**Conclusion:** NIR fluorescent organic probes, through advanced bioengineering and photostable design, are reshaping tumor resection practices, allowing for more precise and complete removal of cancerous tissues. As research progresses, integrating this technology into routine clinical practice seems promising, offering improved patient outcomes. Further clinical trials and technological advancements will be critical to fully realizing the routine use of NIR probes in cancer surgery.

**Acknowledgments:** We express our sincere gratitude for the funding provided by the European Commission under the project titled "Nanoparticles in Environment and Medical Research" (NanoKos - 438247)

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# Comparative Study on the Corrosion Inhibition Efficiency of 2-Hydroxyethyl Trimethyl Ammonium Chloride (HETMAC) and 2-Hydroxyethyl Trimethyl Ammonium Acetate for 6082 Aluminum Alloy in Saline Environments

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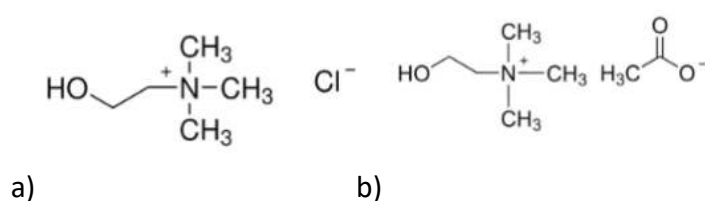
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## Abstract

This study evaluates the effectiveness of two quaternary ammonium salts, i.e., 2-hydroxyethyl-trimethyl-ammonium chloride (HETMAC) and 2-hydroxyethyl-tri-methyl-ammonium acetate (HETMAA), as corrosion inhibitors for 6082 aluminium alloy exposed to a 3.5% NaCl solution. The performance of these inhibitors was assessed using potentiodynamic polarization and electrochemical impedance spectroscopy (EIS) techniques. Both HETMAC and HETMAA exhibited moderate corrosion inhibition of aluminium in saline solution, with their maximum efficiency observed at a 5 mM concentration. However, the data obtained from the Tafel extrapolation of the potentiodynamic curves clearly show a significant difference in the corrosion inhibition efficiency of the two quaternary ammonium salts (i.e., 31.35% for HETMAC and 70.51% for HETMAA. Both corrosion inhibitor act as mixed type inhibitors, HETMAA has dominance on anodic site and HETMAC has dominance on anodic site. The difference in the corrosion inhibition performance is due to the presence of acetate anion present in HETMAA compound compared to chlorine anion in HETMAC compound. EIS measurements revealed a notable increase in charge transfer resistance upon the addition of the inhibitors compare to blank solution, indicating the formation of a protective layer on the 6082 aluminium alloy surface. HETMAA enhances the corrosion resistance of 6082 aluminium alloy. These findings suggest that HETMAA is the preferred inhibitor for protection of aluminium 6082 in saline environment compared to HETMAC.



**Figure 1:** The chemical structures of: a) 2-hydroxyethyl-trimethyl-ammonium chloride (HETMAC) and b) 2-hydroxyethyl-tri-methyl-ammonium acetate (HETMAA).



# Leveraging Microfluidic Technology as a Tool for Production of Lipid Nanoparticles for Nucleic Acids Delivery

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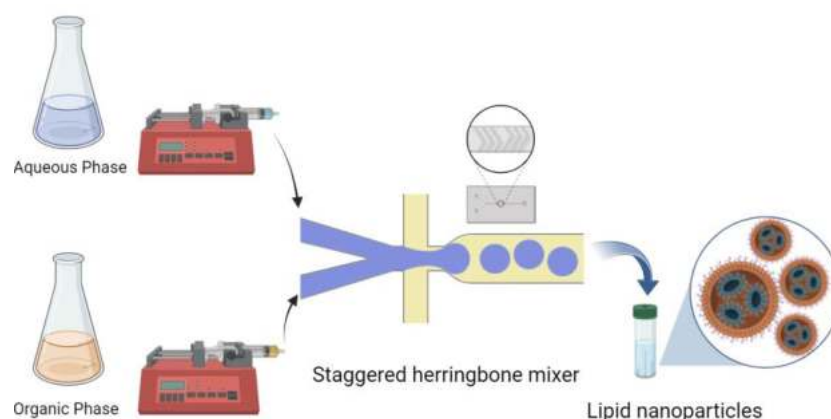
## Abstract:

Lipid nanoparticles (LNPs) are essential for the effective delivery of nucleic acids in gene therapy and molecular medicine. Composed of ionizable, helper, and PEG-lipids, LNPs encapsulate and protect RNA and DNA, preventing degradation, enhancing cellular uptake, and facilitating intracellular release. This technology has greatly contributed to RNA-based therapeutics, playing a key role in vaccine development and treatments for cancer, infectious diseases, and genetic disorders. This research focuses on encapsulating non-coding RNAs and plasmid DNA using microfluidic techniques to achieve high encapsulation efficiency, uniform particle size, and stable formulations [1]. Microfluidics, which controls fluid movement in microscale channels, offers precise production of LNPs. This method allows for control over particle size and encapsulation efficiency, which are critical for the performance of nano delivery systems [2]. LNPs for RNA (siRNA and miRNA) were prepared by dissolving lipids in ethanol and mixing with an aqueous buffer using a herringbone microfluidic mixer. DNA plasmid LNPs followed a similar process with different lipid ratios and buffers. The resulting LNPs were purified and lyophilized. Characterization showed RNA LNPs ranged from 100-120 nm and DNA plasmid LNPs from 150-200 nm, achieving 60% to 80% encapsulation efficiency. Stability tests at 4°C showed that LNPs maintained size and encapsulation integrity. In vitro assays demonstrated effective cellular uptake, with siRNA achieving gene silencing in pancreatic beta-cells and plasmid DNA showing up to 90% transfection efficiency in HEK293T and HeLa cells. In summary microfluidic techniques enable efficient encapsulation of RNAs and plasmid DNA in lipid nanoparticles, enhancing the efficacy of nucleic acid-based therapeutics.

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**Figure 1:** Graphical presentation of microfluidic production of LNPs encapsulating RNA and pDNA

# Advancements in Nanoformulations of Thymol and Chlorothymol: Characterization, Comparative Studies and Stability Enhancement

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This research investigates the formulation and characterization of nanosystems, specifically nanoemulsions and nanostructured lipid carriers (NLCs), incorporating the active compounds thymol and chlorothymol. Various formulations were developed through high-pressure homogenization, utilizing both nanoemulsions and NLCs.

The study compares two types of NLC formulations—one with 1% surfactant and the other with 4%—combined with varying concentrations of thymol and chlorothymol. Comprehensive characterization techniques were employed, including particle size analysis, zeta potential, and morphological assessments, along with dissolution profiles, rheological properties, and surface tension measurements. Stability studies conducted over 1 day, 2 weeks, and 4 weeks provided insights into the physicochemical properties of these nanoformulations.

The results indicate that tailored nanoformulation strategies can significantly enhance the stability and therapeutic potential of thymol and chlorothymol in targeted applications.

Both thymol and chlorothymol nanoformulations produced nano-sized particles. Nanoemulsions had particle sizes of 70-120 nm, NLCs with 1% surfactant ranged from 60-80 nm, and those with 4% surfactant were around 200 nm.

These findings suggest that the stability and therapeutic potential of thymol and chlorothymol can be greatly enhanced by customized nanoformulation techniques.

**Keywords:** nanoemulsions, nanostructured lipid carriers, high-pressure homogenization, stability, thymol, chlorothymol.

Mimoza Basholli-Saliu, Aida Loshaj-Shala, Toskë Kryeziu, Fatbardha Halilaj, Rrona Pozhari and Stina Morina are members of NANOALB research group.

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## Abstract

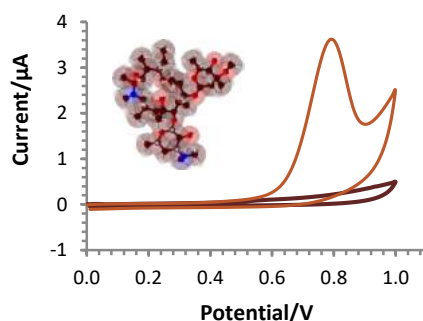
Azithromycin (AZT) is part of the antibiotics called macrolides [1,2], it is widely used medicament, whereby it is expected to be found as a pollutant in environmental waters. Since it is a common medicament, it is important also its analysis in body fluids. Electrochemical methods, although restricted by the fact of the molecules being electrochemically active, are very convenient due to the simplicity of the analysis setup and low cost. Thus the investigation of the electrochemical properties of the molecules of interest becomes very important, both for their analysis and their electrochemical removal from waters [2,3]. In this work the electrochemical behaviour of AZT is presented along with an elaboration on electrochemical active site of the molecule on screen printed carbon electrode (SPCE). A potentiostat Palmsens4 was used for the measurements. To shed more light on the mechanism of AZT oxidation mechanism, cyclic voltammograms of some similar atomic group bearing simpler molecules were recorded. It was further elaborated the nitrogen as centre of activity by comparing the voltammograms of AZT with other the molecules. The electrochemical oxidation was controlled partly by electron transfer and diffusion. The pH value influenced greatly the peak current and it was the highest at pH 10.

**Keywords:** Carbon, electrochemical oxidation, Azithromycin, voltammetry, mechanism.

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## Figures



**Figure 1:** Cyclic voltammogram of [AZT] = 50 ppm on SPCE, pH = 8.5, scan rate = 0.05 V/s.

# Physico-mechanical and mineralogical characterization of ceramics obtained from diatomite earth

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## Abstract

In this work, it is intended that diatomaceous earth be used as a material for the production of ceramics. Taking in consideration that the DE is mined from geological deposits, it may contain certain impurities such as metal oxides and organic matter, which may have particular effects towards its application properties. The chemical composition of diatomaceous earth is predominantly silica (SiO<sub>2</sub>). One way to improve the properties of DE is through the sintering process. During the sintering process, the impurities are removed followed by mineralogical changes that results in the enhancement on the characteristics of diatomite. For the purpose of sintering, the DE was first crushed and ball-milled for a period of 2.5 h. After the pulverization of the material, the samples were sintered at 1000°C temperature, for a period of 1h, 2h and 3h. After the thermal treatment, physico-mechanical and mineralogical analyzes will be performed to analyze the influence of temperature and treatment time on the ceramic samples. Concretely, the bulk density will be determined, then the topography or surface homogeneity of the samples will be studied by means of optical microscopy. Furthermore, the mechanical properties of the samples such as hardness and commpressive strength are studied in dependence of sintering time and temeprature.

*Keywords: Diatomaceous earth; Characterization; Sintering, temperature*

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# Impact of modified coal with organic layer on the performance of reverse osmosis heterogeneous asymmetric Cellulose Acetate Membranes

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Kosovo's lignite coal particles were tethered with alkyl or mixed alkyl-aryl layers by diverting the reactivity of aryl radicals, derived from aryl diazonium salts, with alkyl halides. [1] The modification is performed in aqueous acid medium when a mixture of aryl diazonium salt and alkyl halide compound of 20 mM concentration with or without using a chemical reducing agent. [2] The presence of organic layer is attested by Attenuated Total Reflectance Fourier-Transform Infrared (ATR-FTIR) spectroscopy which revealed the presence of characteristic groups of used compounds. [1] Modified coal is used to prepare cellulose acetate heterogeneous asymmetric reverse osmosis membranes. The morphology of such membranes is characterized with Scanning Electron Microscopy, SEM. [3] Measurements of different membrane parameters were made in an aqueous solution of sodium chloride as a referent system of feed concentration  $c = 6.8 \times 10^{-3} \text{ mol dm}^{-3}$  at 1.763 MPa. Heterogeneous asymmetric membranes prepared with modified coal have shown much better performance regarding reverse osmosis parameters: increased permeability, rejection capability, product rate, and solute separation as well. The modification procedure of coal particles with organic layer in aqueous acid solution can be easily implemented and may be widely applicable in water treatment and desalination.

**Key words:** Modified coal particles, alkyl and mixed alkyl-aryl layer, heterogeneous asymmetric membranes.

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# Development of Advanced Biomimetic Hybrid Liposomes via Microfluidics for Enhanced Targeted Delivery and Antitumor Activity in Glioblastoma Cells

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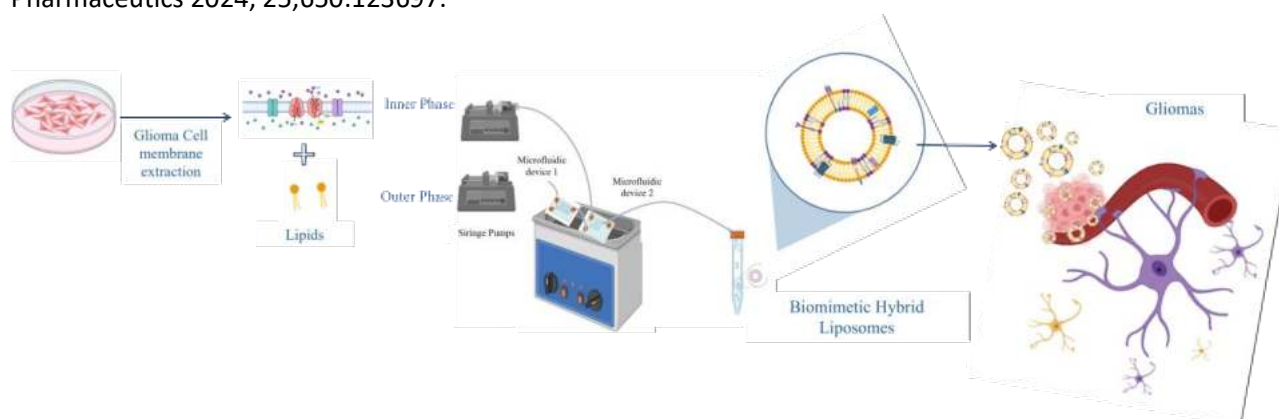
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## Abstract

The treatment of glioblastoma faces significant challenges primarily due to the blood-brain barrier (BBB) and the rapid immune clearance of drugs, underscoring the urgent need for advanced delivery systems. [1] This study aims to investigate an innovative drug delivery method using paclitaxel and carboplatin encapsulated in specially bioengineered liposomes. By incorporating cell membrane (CM) fragments extracted from a glioblastoma cell line into the liposomes, we aimed to endow them with stealth properties, improve their targeting efficiency, and enable them to evade immune detection. This modification allows the liposomes to accumulate in tumours through homotypic targeting preferentially.[2] Microfluidic technique was employed to produce these biohybrid liposomes (Figure 1), namely we developed a microfluidic sonication method that integrates active and passive mixing techniques to enhance nanoparticle production efficiency. [3] Specifically, we employed two approaches: 1) using a single device placed in a sonicator bath for cell membrane (CM) breakdown, and 2) using two devices in series, where device 1 was placed in a sonicator bath for CM breakdown and device 2 was used for nanoparticle (NP) formation. To assess hybridization and confirm successful membrane fusion, we performed Förster resonance energy transfer, colocalization studies by flow cytometry, and Western blotting techniques. In vitro studies confirmed that these biomimetic hybrid liposomes can effectively target tumors, cross the BBB, and maintain the efficacy of paclitaxel and carboplatin. This novel delivery system offers a promising non-invasive approach for glioblastoma treatment, potentially eliminating invasive procedures to achieve effective drug delivery across the BBB.

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**Figure 1:** Scheme of the microfluidic production of biomimetic hybrid liposomes.

# Comparison of two methods for graphene oxide nanomaterials synthesis for the analyte signal production

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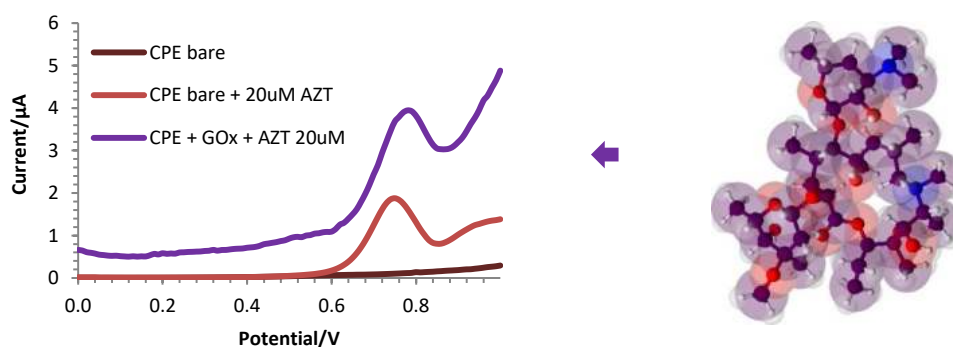
## Abstract

Carbon based materials are widely used for electrochemical sensing as well as anodes for electrochemical removal of organic pollutants from aquatic media [1,2]. Graphene has attracted a lot of attention for electrochemical applications, due to its characteristic physico-chemical properties. In this work graphene oxide nanomaterials were synthesized by electrochemical exfoliation and the modified Hummer's method [3]. The obtained nanomaterials were applied comparatively as modifiers for carbon paste working electrode for cyclic voltammetry of azithromycin (AZT) in phosphate buffer (PBS) at pH 8.5 [4]. The material was prepared in the form of paste and lodged into the teflon holder. Both materials produced improved voltammetric peaks for AZT, in comparison to carbon paste electrode.

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## Figures



**Figure 1:** Voltammogram of azithromycin. [AZT] = 50  $\mu$ M, Scan rate = 0.05 V/s, PBS pH = 8.5.



# A mapping of the distribution of the albanian wine quality based on their antioxidant capacity.

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## Abstract

This study presents a comprehensive mapping of Albanian wine quality based on their antioxidant capacity, with a focus on catechin quantification using modified carbon paste electrodes (CPE). Because wine composition is so complicated, it is difficult to determine catechins directly, which is why an ex-situ voltametric approach was developed. Using this technique, the CPE is extracted or adsorbed upon, and then differential pulse voltammetry (DPV) measurements are made. The CPE was modified using a variety of nanomaterials, with multi-walled carbon nanotubes (MWCNTs) showing the highest sensitivity. Other nanomaterials that were employed included zeolite, Prrenjasi clay, and carbon nanotubes. Albanian wines have 665–2235 mg/L of catechins, with red wines having higher antioxidant contents than white wines. A comparative examination using UV-VIS spectrophotometry and the Prussian blue spectrophotometric approach, both of which showed consistent patterns, validated the results. Climate and soil composition have been discovered to have a major impact on antioxidant content; warmer climates are associated with higher antioxidant capacity in wines. This approach offers Albanian wine producers a useful tool for evaluating and accrediting wine quality according to antioxidant content.

# Cytotoxic and Oxidative Stress Responses to Differently Charged and Sized Microparticles in Caco-2 Cells

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Nanoparticles and microparticles are increasingly utilized in various fields, including biomedicine and environmental science. It is essential to assess their potential cytotoxicity and ability to induce oxidative stress to ensure their safe application. This study explores the effects of five engineered microparticles, differing in charge and size, on Caco-2 cells, a human epithelial colorectal adenocarcinoma cell line.

Cytotoxicity was evaluated using the CCK-8 (Cell Counting Kit-8) assay to measure cell viability following exposure to five distinct microparticles: positively charged MF, neutral PS, negatively charged SD, and two PS particles of varying sizes (1  $\mu\text{m}$  and 0.1  $\mu\text{m}$ ). Cells were treated with each particle, and the results were quantified based on absorbance readings, allowing for the determination of the relative viability of the cells in response to each treatment.

To assess oxidative stress, the Cell Meter™ Fluorimetric Intracellular Total ROS Activity Assay Kit was used. ROS production in Caco-2 cells was measured via flow cytometry following microparticle exposure, with a specific focus on correlating particle characteristics (charge and size) with their ability to induce ROS generation.

The cytotoxicity data revealed distinct particle-specific effects, with variations in cell viability observed based on particle charge and size. Positively charged and smaller particles exhibited a more pronounced reduction in cell viability compared to neutral or larger particles. Similarly, the ROS measurements demonstrated a differential induction of oxidative stress, with charged particles, particularly those with positive surface charges, showing higher ROS generation compared to neutral and negatively charged particles.

This study aimed to explore the varying cytotoxic and oxidative stress profiles of engineered microparticles in Caco-2 cells, highlighting the influence of particle charge and size. There are few reports for differently charge nano- or micro-particles inducing cytotoxicity in cell lines. Therefore, this study aimed to better understand the cytotoxicity of differently charged nano- or micro-particles in Caco-2 cells.

These findings provide important insights into the biological impact of these particles, with potential implications for their use in pharmaceuticals, consumer products, and environmental applications.

Keywords: Nanoparticles, microparticles, cytotoxicity, Caco-2 cells, particle charge, particle size, ROS .

## Acknowledgments

We express our sincere gratitude for the funding provided by the European Commission under the project titled "Nanoparticles in Environment and Medical Research" (NanoKos - 438247)

# Removal of methyl blue and bromophenol blue by Fenton process from aqueous solution

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## Abstract

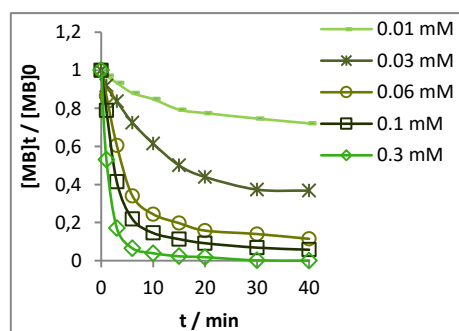
Chemical pollution is present nowadays commonly in surface waters and in other environmental areas as well [1–3]. Of particular importance are organic compounds, which are synthesized in large variety, whereby their harmful potential and unpredictability of their toxic properties towards various organisms. Dyes are considered among the main organic pollutants of waters. The removal of Methyl Blue (MB) and Bromophenol blue (BPHB) from aqueous solution by Fenton process [4] was considered in this work. Removal efficiency was studied as well as the rate constants of the reactions were determined. The degradation was performed in a 150 mL beaker under stirring conditions at pH 3. The kinetics of the compounds degradation was followed by UV-Vis spectrophotometry. It was found that both compounds can be effectively degraded, whereas MB is degraded more rapidly than BPHB. The pH reduced the efficiency of the degradation process, but even at pH 5.2 significant amounts of the both compounds could still be oxidized, due to the pH decrease during the process, probably effected by the carboxylic acids formed during the degradation process.

**Keywords:** Pollution, Fenton, dyes, removal, environment.

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## Figures



**Figure 1:** Degradation trails of MB at different concentrations of  $[H_2O_2] = [Fe^{2+}]$ ,  $[MB]_0 = 0.01$  mM,  $V = 150$  mL,  $pH = 3$ .

## Exploring encapsulation of berberine into nanoparticles utilizing microfluidic technique

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Berberine, an isoquinoline alkaloid present in various plant species including Berberis, offers diverse health benefits, albeit hindered by poor aqueous solubility, limited absorption, and low bioavailability. To surmount these challenges, the application of nanotechnology has been contemplated. In order to encapsulate this substance, the microfluidic technique was employed. In our efforts to encapsulate berberine in liposomes, we have conducted measurements for size, polydispersity index (PDI), count, intensity, zeta potential, and encapsulation efficiency (EE) to better track our progress in this project. The liposomes produced using the microfluidic technique had an average size of 115.41 +/- 9.17, indicating a relatively uniform particle size, a polydispersity index (PDI) of 0.293 +/- 0.02 suggests a wide range of particle sizes within the formulation. Furthermore, the encapsulation efficiency was measured at 76%, signifying the effectiveness of the liposomes in encapsulating the desired substances. In conclusion, the encapsulation of berberine in liposomes has demonstrated success through the implementation of the microfluidic technique. This method offers precise control and uniformity in the encapsulation process, potentially contributing to advancements in drug delivery and the bioavailability of berberine.

**Keywords:** berberine, poorly water-soluble, encapsulation, nanoparticles, liposomes, microfluidic technique.

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# Design and synthesis of some novel compounds derived from hybrid coumarin-thiazole structures

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## Abstract

Coumarins are molecules that belongs to a special family of compounds which, due to the conjugated double bond become interesting molecules for many fields of study. Their structure and physical properties make them a privileged scaffold in medicinal chemistry. Also, they exhibit a wide range of biological activity including free radical scavenging. Recent research has focused attention on the anticancer activity of coumarin and coumarin- derived compounds due to their high level of cytotoxicity. Thiazole rings, on the other hand, had also showed remarkable anticancer activity on various cancer cells. Based on this, the idea was to combine those two heterocyclic units in one hybrid unique molecular structure with high anticancer potential. The synthetic strategy was simple, applying the reaction of diazotation of 2-aminothiazoles and using the corresponding diazonium salts as good electrophiles to attack the 4-hydroxycoumarin at position 3. Furthermore, it was revealed by previous investigation that the alkyl substituent at the thiazole ring is playing key role. Namely, by increasing of the nonpolar tail at that part of the molecule, the biological activity is also increased. Based on this, some 4-substituted-2-aminothiazoles were synthesized by optimization of the Hantzsch reaction, prior to diazotation and coupling with the coumarin core. All of the newly synthesized compounds were purified by crystallization and the melting point was determined. Finally, the obtained compounds were characterized by spectroscopic means.

*Keywords:* synthesis, coumarin, thiazole, Hantzsch reaction, anticancer activity

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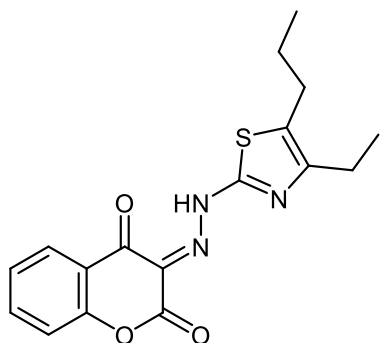
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## Figures



**Figure1.** Structure of novel coupling derivative

# Design and synthesis of some novel compounds derived from hybrid coumarin-sulfonamides structures

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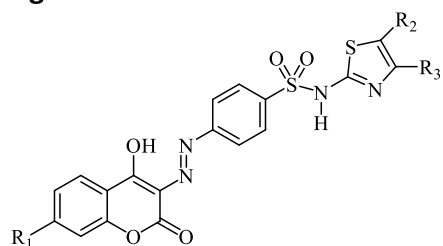
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**Abstract.** Coumarin, a natural benzopyrone derivative, has garnered significant attention in the field of medicinal chemistry due to its diverse pharmacological properties. Known for their anticoagulant, anti-inflammatory, antimicrobial, and antioxidant activities, coumarins have emerged as promising candidates for drug development. One notable structural modification involves also the incorporation of sulfonamide groups, adding a distinct dimension to the pharmacological profile. Understanding the synergistic effects between coumarin and sulfonamide groups provides valuable information for designing novel therapeutic agents.

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## Figures



**Figure 1.** General structure of new syntheses



## COMPARATIVE BIODISTRIBUTION OF EXOSOME, LIPID NANOPARTICLE, AND HYBRID FORMULATIONS FOR TARGETED GASTROINTESTINAL DELIVERY OF ANTI-TNF ALPHA

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**Background:** Drug delivery systems are crucial for enhancing the impact of medical treatments, particularly when focusing on tissues such as those of the gastrointestinal (GI) tract. Formulations like exosomes, lipid nanoparticles, and hybrids, have shown promising drug delivery vehicles for site-specific delivery of biologics such as anti-TNF alpha, a therapeutic agent that has been used to treat inflammatory diseases. Studying the bioavailability of these targeted drug delivery systems, could lead to remarkable improvement of medicinal outcomes including targeted treatment of the gastrointestinal tract (GI).

**Aim:** Our objective was to explore the GI biodistribution of three drug delivery systems-exosomes, LNP, and hybrids encapsulating the anti-TNF alpha factor.

**Methods:** Formulations of interest which include exosomes, LNP, and hybrids were administered to the mice. The biodistribution and intensity of bioavailability have been measured at time marks: 2h, 4h, 8h, and 24h post-administration using the Pearl LI-COR imaging system. At the 24-hour mark, the mice were dissected, and the intensity of the formulations was further measured in key organs of the gastrointestinal (GI) tract.

**Results:** The hybrid formulation showed the highest uptake and signal intensity, followed by LNP and exosomes. Each formulation showed a steady decline signal intensity from its peak two hours after dosage throughout the duration of 24 hours period. Compared to exosomes and LNPs, the hybrid system showed better biodistribution in the gastrointestinal (GI) tract.

**Conclusion:** The hybrid drug delivery system showed the most effective retention and distribution within the gastrointestinal tract, suggesting that it may be a superior formulation for the localized delivery of anti-TNF alpha in the treatment of inflammatory gut diseases. Further research is needed to optimize these formulations for clinical use.

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### Acknowledgments

We express our sincere gratitude for the funding provided by the European Commission under the project titled "Nanoparticles in Environment and Medical Research" (NanoKos - 438247).

## Enhancing the Antioxidant and Anticancer Potential of *Lavandula angustifolia* Essential Oil through Nanoformulation and Storage Evaluation

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*Lavandula angustifolia*, commonly known as lavender, is a well-known medicinal plant with numerous therapeutic benefits. Its essential oil is rich in bioactive compounds, including antioxidants and phytochemicals that exhibit promising anticancer/cytotoxic activities.

The study aims to optimize the therapeutic efficacy of *L. angustifolia* essential oil by employing a nanoformulation approach (liposomes and nanoemulsions). Nanoformulations have gained considerable attention in recent years due to their ability to enhance the bioavailability and stability of therapeutic agents. By encapsulating the essential oil within nanoparticles, its bioactivity can be preserved, and potential issues such as volatility and degradation can be minimized.

The presentation discusses the nanoformulation of *L. angustifolia* essential oil-loaded nanoparticles using biocompatible and biodegradable materials. Various characterization techniques, including particle size analysis, zeta potential determination, and encapsulation efficiency evaluation, were employed to assess the physicochemical properties and stability of the nanoformulation. Additionally, *in vitro* human cancer cells viability studies were conducted to investigate the controlled release behaviour of the essential oil from the nanoparticles.

Furthermore, the storage stability of the nanoformulation was evaluated under different conditions to assess its long-term stability. The changes in particle size, zeta potential and encapsulation efficiency of the essential oil were monitored over time to determine the impact of storage conditions on the nanoformulation.

The results indicate that the nanoformulation successfully encapsulated *L. angustifolia* essential oil, preserving its antioxidant and anticancer potential. Moreover, the stability studies revealed the importance of proper storage conditions to maintain the integrity and bioactivity of the nanoformulation.

Overall, this oral presentation highlights the potential of nanoformulation as a strategy to enhance the antioxidant and anticancer properties of *L. angustifolia* essential oil. The findings contribute to the development of innovative and efficient delivery systems for natural products, opening new avenues for their therapeutic applications in the field of cancer treatment and prevention.

The authors are grateful to the CEEPUS/OeAD mobility programme for providing financial support (scholarship) to Toskë Kryeziu.

Toskë Kryeziu and Mimoza Basholli-Saliu are members of NANOALB research group.

# The utilization of state-of-the-art graphene derivatives in electrochemical sensor technology for the detection of neonicotinoids

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Neonicotinoids, widely used herbicides in agriculture, have become a key focus of research due to their potent acute toxicity and neurotoxic effects resulting from prolonged exposure <sup>[1]</sup>. The main goal of this study is to develop an innovative electrochemical sensing material using state-of-the-art graphene derivatives <sup>[2][3]</sup> for monitoring neonicotinoids level in the environment. To achieve this goal, we selected and evaluated four graphene derivatives—graphene acid (GA), graphene acid with iron nanoparticles (GAFe), nitrogen-doped graphene (GN3) and cyano-graphene (GCN) —as potential candidates for detecting structurally similar pesticides <sup>[4,5]</sup>. The sensor was characterized using electrochemical impedance spectroscopy (EIS), cyclic voltammetry (CV) and square-wave voltammetry (SWV). The results indicate that these derivatives exhibit improved analytical performance compared to a bare glassy carbon electrode (GCE), which can be attributed to their high conductivity and enhanced electron transfer ability on the electrode surface. Optimization of the square-wave voltammetry technique and pH value was carried out using a factorial design. The GCE/GAFe-based sensor demonstrated a significant electrochemical response to paraquat (PQ), with a sensitivity of 0.07 (μA/mM), correlation of 0.984, and a linear range of 0.05 to 1. 25mM. These findings highlight the potential of graphene-based materials for efficient and sensitive detection of neonicotinoids and structurally related pesticides, such as paraquat, thiamethoxam, and imidacloprid.

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According to many studies, BRCA genes are considered polymorphic and BRCA variants are highly deleterious in damaging BRCA function, causing genome instability and increased cancer risk, affecting mostly breast and ovaries [1], [3]. This study aims to investigate the spectrum of BRCA1 and BRCA2 genetic variants in female Albanian population and to analyze the mutations significance from an evolutionary perspective. The national screening of women for breast cancer is done through imaging techniques at Obstetrics and Gynecological University Hospital (Queen Geraldina), in Tirana, Albania (almost 600 tests/year). BRCA gene variants will be identified through Multiplex Ligation Probe Assay (MLPA) and fragment analysis will be done with SeqStudio genetic analyser. These variants will be compared with the documented identified variants, to define the pathogenic variants. Actually, a family of 6 women members, already identified by MLPA assay with a deletion in exon 11 of BRCA1 gene, will be included in the positive control group. These tests demonstrated the existence of an autosomal dominant pattern of inheritance of the breast cancer cases, that is already confirmed by other studies. Furthermore, extensive studies suggest that BRCA genes vary by ethnicity [4]. This is very important to study in Albanian population, as this country has its unique genetic, linguistic, and cultural features [2]. Evolution factors contributed to this ethnic specificity, which include the positive selection imposed on human BRCA genes, the adaptation of different ethnic populations to their living environment, the bottleneck and founder effects, will also be involved in this study. As the studies suggest, this investigation is of highly importance in providing genetic evidences to understand the relationship between human evolution and cancer risk [4]. Finally, this study may contribute to provide an overview of Albanian population for the BRCA variation genes and a comprehensive reference for clinical applications in the era of precising medicine.

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# Electrochemical Graphene-Based Immunosensor for Accurate Detection of Small Molecules

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Our research focuses on harnessing the unique properties of graphene-based nanomaterials and antibodies to develop enhanced immunosensor devices. We employ a sustainable, cost-effective, one-step printing and stamping method to fabricate nanostructured three-electrode electrochemical cells. This process involves the use of an infrared laser to precisely exfoliate and reduce graphene oxide (rGO), which can be transferred onto flexible substrates like PET to yield electrodes [1]. The working electrode is functionalized with monoclonal antibodies [2] or nanobodies to selectively capture and detect small molecules. Upon analyte binding to the immobilized antibodies, dose-dependent electrochemical signals are produced, enabling rapid and accurate detection of small molecules. This integration of nanomaterials, biosensors, and electrochemical techniques holds significant promise for rapid detection of small molecules in the field of healthcare and food safety.

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# Nano-Therapeutics to Treat Acne Vulgaris: Improved Therapeutic Efficacy and Skin Tolerability

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Nano-therapeutics for treating Acne Vulgaris represent a cutting-edge approach in dermatological care, leveraging the advancements in nanoscale drug delivery systems (NDDS) to enhance therapeutic efficacy and skin tolerability. This abstract outlines the exploration of novel nano-based treatments for acne, focusing on their development, mechanisms, and potential to improve patient outcomes significantly.

The core of this exploration is the innovative use of nano-therapeutics, including liposomes, nanoemulsions, solid lipid nanoparticles, and polymeric nanoparticles, specifically tailored for combating Acne Vulgaris. These systems offer unprecedented advantages in drug delivery, such as increased penetration of active ingredients into the skin, targeted action on acne-causing bacteria and inflamed tissues, and controlled release of therapeutics, thereby minimizing systemic absorption and associated side effects.

Critical to the advancement of these nano-therapeutics is the emphasis on biocompatibility and skin tolerability. The presentation delves into the selection of materials and design principles that ensure compatibility with skin physiology, reducing irritation and enhancing patient compliance. Innovative strategies for improving the stability and efficacy of active ingredients against the harsh skin environment are also discussed, including encapsulation techniques and surface modification of nanoparticles.

The challenges of quality control and safety in the development of nano-therapeutics for acne are addressed comprehensively. We analyze the methods for characterizing nanoparticle formulations, assessing their physical stability, skin permeability, and biodistribution, as well as the importance of conducting rigorous toxicological evaluations to ensure safety for topical use.

In conclusion, nano-therapeutics hold great promise for revolutionizing the treatment of Acne Vulgaris, offering improved therapeutic efficacy and skin tolerability. This research underscores the need for a multidisciplinary approach, involving collaboration among dermatologists, pharmaceutical scientists, and regulatory bodies, to overcome the challenges in quality control and safety assurance, paving the way for their successful integration into dermatological practice.

Venesa Lupçi and Toskë Kryeziu are members of NANOALB research group.

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Integrating nanotechnology into pharmaceuticals has significantly advanced drug delivery systems, particularly by developing nanoparticles (NPs) that enhance the pharmacokinetic properties of therapeutic agents. This review explores the current landscape of nano-pharmacokinetics, highlighting the benefits of nanoparticle formulations in improving drug solubility, stability, and targeted delivery, especially in complex disease treatments such as cancer. A systematic literature review was conducted using PubMed, EMBASE, and Cochrane databases, focusing on studies published up to September 2024. Keywords regarding the nanodrugs and pharmacokinetic parameters were used. The findings reveal that nanoparticle-loaded drugs exhibit superior pharmacokinetic profiles compared to traditional formulations, characterized by increased area under the curve (AUC), enhanced bioavailability, and prolonged circulation times. Notably, engineered nanoparticles demonstrate the ability to bypass biological barriers and address multidrug resistance through innovative combination therapies. Looking ahead, the future of nano-pharmacokinetics lies in precision medicine, where intelligent nanoparticles are designed to respond dynamically to patient-specific factors and tumor microenvironments. This evolution promises to optimize therapeutic efficacy while minimizing adverse effects and improving patient outcomes. Continued research and clinical trials are essential for translating these advancements into practical applications in healthcare.

Amir Makolli and Mimoza Basholli-Salihu are members of NANOALB research group.



# Thin Film Electrodes Based on Zn<sub>2</sub>SnO<sub>4</sub> on In<sub>2</sub>O<sub>3</sub> Substrates Developed for Electrochemical Determination of Dopamine

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## Abstract

Thin films provide several advantages for biosensors, such as high surface-to-volume ratio, conductivity, stability, specificity, biocompatibility and strong electrochemical activity, depending on the material used. The electrodes of biosensors are modified with thin film coatings. These thin film-modified electrodes act like transducers, possessing physicochemical properties such as electrical, magnetic, mechanical, and optical characteristics. As a result, the signal generated from the analyte-electrode interaction can be converted into a measurable signal [1]. In recent advancements in biosensor technology, thin film electrodes have emerged as a significant area of development. Dopamine (DA) plays a crucial role in the onset and management of various diseases, including Alzheimer's and Parkinson's. Consequently, monitoring DA levels is essential, and biosensors offer a promising alternative to traditional methods, which are often time-consuming and costly [2,3]. This study, we present the application of Zn<sub>2</sub>SnO<sub>4</sub> (ZTO) deposited onto an In<sub>2</sub>O<sub>3</sub>:SnO<sub>2</sub> (ITO) thin film as the electrode platform for biosensing applications targeting DA [4]. The ZTO thin film was deposited using the DC magnetron sputtering technique with a Zn<sub>2</sub>Sn (ZT) target and O<sub>2</sub> gas. Electrochemical analysis were performed using cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), and differential pulse voltammetry (DPV). Electrochemical results indicated that these developed electrodes successfully applied for sensitive determination of DA. Additionally, experiments conducted in the presence of potential interfering substances such as ascorbic acid (AA), uric acid (UA), bovine serum albumin (BSA), and fish sperm double-stranded DNA (fsDNA) demonstrated that the electrodes could effectively be used for the voltammetric determination of DA.

**Acknowledgements:** The authors acknowledge Research and Application Center for Quantum Technologies (RACQUT) for the facilities of IZTECH they provided for this study. Arzum Erdem Gürsan would like to express her gratitude to the Turkish Academy of Sciences (TÜBA) as a principal member for its partial support.

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# Nanocarrier Applications for Beta-Thujaplicin Encapsulation: Characterization and Stability Insights

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## Abstract

$\beta$ -Thujaplicin, also known as hinokiol, is a naturally occurring monoterpenoid found in the heartwood of trees from the *Cupressaceae* family, recognized for its broad-spectrum antimicrobial, antiviral, and antioxidant activities. Despite its therapeutic potential,  $\beta$ -thujaplicin's poor water solubility and degradation susceptibility limit its pharmaceutical applications.

To overcome these challenges,  $\beta$ -thujaplicin was encapsulated into two nanoscale delivery systems—nanoemulsions and nanostructured lipid carriers (NLCs)—to enhance its stability and biological activity.

Nanoemulsions, colloidal systems with oil droplets dispersed in water, improve the solubilization of hydrophobic compounds like  $\beta$ -thujaplicin, offering enhanced absorption and bioavailability. NLCs, lipid-based carriers, allow for controlled drug release and improved drug loading. Both systems provide protection from degradation and enable targeted delivery.

Characterization of the formulations, performed using a Malvern Zetasizer, showed particle sizes between 80 and 140 nm, with polydispersity index (PDI) ranging from 0.10 to 0.20, indicating uniform particle distribution. Zeta potential analysis confirmed good colloidal stability for both nanoformulations. Stability studies revealed minimal changes in particle size and PDI over time, highlighting the long-term stability of both nanosystems. These results suggest that  $\beta$ -thujaplicin can be successfully formulated into nanoemulsions and NLCs, providing promising platforms for enhanced drug delivery. Future research will focus on *in vitro* and *in vivo* evaluation to explore their clinical potential.

**Keywords:** nanoemulsions, nanostructured lipid carriers, characterisation, stability,  $\beta$ -thujaplicin

\*Mimoza Basholli-Salihu, Aida Loshaj-Shala, Toskë Kryeziu, Rrona Mehmeti, Stina Morina, Fatbardha Halilaj and Rrona Pozhari are members of NANOALB research group.

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# Comprehensive Analysis of Troponone Nanoformulations: Characterization and Assessment of Antioxidant Activity

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Tropolone, a naturally occurring compound known for its potent antioxidant properties, holds significant therapeutic potential. However, its practical application is limited by challenges such as low solubility and thermal instability, particularly due to its low boiling point (80–84°C), which can lead to degradation during processing.

This study addresses these challenges by developing and formulating two lipid-based nanocarriers: nanoemulsions (NE-Trop) and nanostructured lipid carriers (NLC-Trop). These formulations aim to enhance the delivery and stability of tropolone. The results indicate a notable improvement in stability and antioxidant activity.

Using a high-pressure homogenizer during the nanoformulation process, we ensured uniform particle size and stability, employing temperature control to minimize thermal degradation. Characterization of the formulations revealed particle sizes ranging from 50 nm to 80 nm, demonstrating suitable stability for pharmaceutical applications. Additional assessments of rheological properties and surface tension further validated formulation stability.

The nanoformulations were comprehensively characterized in terms of physicochemical properties, stability, encapsulation efficiency, and antioxidant activity. Our findings highlight a significant enhancement in stability while maintaining its antioxidant potential. This suggests that tropolone-loaded nanocarriers are promising candidates for pharmaceutical applications where enhanced antioxidant properties are essential.

**Keywords:** tropolone, nanoemulsion, nanostructured lipid carrier, antioxidant activity

Mimoza Basholli-Saliu, Aida Loshaj-Shala, Toskë Kryeziu, Stina Morina, Rrona Mehmeti and Fatbardha Halilaj are members of NANOALB research group.

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# Application of various mixing rules in binary mixtures of 1-propanol with benzene and pyridine

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## Abstract

The refractive indices for binary mixtures of 1-propanol + pyridine and 1-propanol + benzene were measured using a calibrated Abbe refractometer (Model G from Carl Zeiss) across the entire mole fraction region at a temperature of 298.15 K and under ambient pressure. In this study, the refractive index mixing rules Arago-Biot (A-B), Lorentz-Lorentz (L-L), Newton (N), and Eyring-John (E-J) were applied to verify their predictive capability for the studied binary systems. The predictive ability was estimated by calculating the average absolute percentage deviation between experimental and calculated values. The findings of the current work demonstrate that refractive index mixing rules can accurately describe the optical properties of binary mixtures, which is crucial in various chemical and industrial processes.

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# In Vitro Assessment of Cytotoxic Effects of Particulate Matter on Isolated Splenocytes and Respiratory Cells

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**Background:** Environmental air pollution, driven largely by particulate matter (PM), is a significant global health concern. PM<sub>2.5</sub> can penetrate the respiratory tract, leading to inflammation and oxidative stress.<sup>1,2</sup> Beyond its impact on the lungs, PM exposure may also disrupt immune functions by affecting organs such as the spleen.<sup>3</sup> Given the spleen's critical role in immune regulation, it is essential to understand how PM<sub>2.5</sub> exposure influences both respiratory and immune health, particularly in regions with high levels of air pollution.<sup>4</sup>

**Aims:** This study aims to evaluate the cytotoxic effects of PM<sub>2.5</sub> on splenocytes and respiratory cells, using samples collected from two cities in Kosovo: Prishtina and Obiliq. We investigated how different concentrations of PM<sub>2.5</sub> affect cellular responses, focusing on the relationship between dose, exposure duration, and cell viability.

**Methods:** Splenocytes and respiratory cells were isolated from the spleens and lungs of mice, respectively. Cells were exposed to culture media containing four concentrations of PM<sub>2.5</sub> (25, 50, 70, and 100 µg/ml) for 24 hours. Cellular viability was measured using MTT assays to assess metabolic activity.

**Results:** Both splenocytes and respiratory cells showed a concentration-dependent decline in metabolic activity after 24, 48 and 72 hours of PM<sub>2.5</sub> exposure.

**Conclusion:** This study underscores the toxic effects of PM<sub>2.5</sub> on both splenocyte and respiratory cell function, providing critical insights into the broader implications of air pollution on human health, particularly its potential to impair both respiratory and immune system function.

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# Graphene derivative-based ink advances inkjet printing technology for fabrication of electrochemical sensors and biosensors

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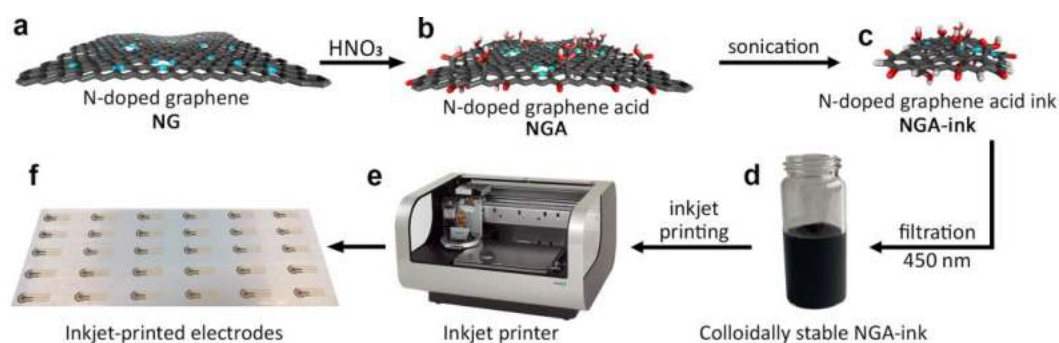
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The development of biosensors could greatly benefit from a new method for producing electrodes via inkjet printing technology, which offers a precise and reproducible manufacturing process. In this regard, we introduce a nitrogen-doped carboxylated graphene ink (NGA-ink), specifically formulated to be compatible with existing inkjet printing systems. This water-based, additive-free ink enables the fabrication of fully inkjet-printed electrodes (IPEs) capable of electrochemical detection of dopamine, an essential neurotransmitter. The cost-effectiveness of NGA-ink, with a total cost per electrode of just \$0.10, makes it a compelling option for on-demand customized electrode production. Additionally, the high carboxyl group concentration (13 wt%) in NGA-ink improves its potential for biomolecule immobilization, thus facilitating the development of advanced biosensors. IPEs made from this ink were fully functional and demonstrated promising electrochemical activity and stability. In summary, the introduction of NGA-ink marks a significant advancement in sensor technology, providing a scalable, cost-efficient, and environmentally friendly solution with improved performance capabilities for advanced biosensing applications. The ability of this ink to enable covalent attachment of biomolecules, such as antibodies or aptamers, opens new possibilities for advanced sensor development and the creation of fully inkjet-printed biosensors.

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## Figures



**Figure 1:** Synthesis of the NGA-ink. Nitrogen-doped graphene (a) is treated with nitric acid, forming carboxyl functionalities. Resulting material, nitrogen-doped graphene acid (b) is filtered and sonicated. Obtained NGA-ink dispersion (c) is filtered through a 450 nm filter to form colloidally stable NGA-ink (d). This ink is then used in printing process utilizing inkjet printer (e). In this way, fully inkjet-printed electrodes (f) can be produced. [1]

# Developing and assessing Carvacrol nanocarriers by High-pressure homogenization: innovating delivery systems for improved stability and antioxidant activity

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This presentation explores the development of innovative nanocarriers aimed at improving the stability and efficacy of carvacrol, a well-known natural antioxidant derived from thyme oil. Despite its numerous health benefits, carvacrol's low solubility and volatility often limit its practical use.

To address these challenges, the high-pressure homogenization was utilized to create lipid-based nanocarriers that effectively encapsulate carvacrol, enhancing antioxidant activity and stability. This study addresses the formulation and characterization of two nanosystems, namely nanoemulsions and nanostructured lipid carriers (NLCs), loaded with carvacrol. Carvacrol, a bioactive compound with known antimicrobial and antioxidant properties, was chosen as the sole active substance. The nanosystems were prepared using distinct methods and compositions, and their physicochemical properties were characterized. Analysis of particle size, zeta potential, drug loading efficiency, and in morphological analysis revealed differences between the nanoemulsions and NLCs, indicating variations in their formulation and potential applications.

The current research demonstrates that encapsulating essential oils in appropriate carriers significantly improves their antioxidant activity and stability. The primary reason why carvacrol-loaded nanoemulsions increase antioxidant activity is because of their larger surface area and smaller particle size, which improves their ability to interact with free radicals. Nanoemulsions offer advantages in terms of smaller particle size and rapid drug release, making them suitable for applications requiring immediate action. On the other hand, NLCs provide higher drug loading efficiency and controlled release profiles, suggesting potential for sustained therapeutic effects.

**Keywords:** carvacrol, nanocarriers, high-pressure homogenization, nanoemulsions, NLC, antioxidant.

Mimoza Basholli-Salihi, Aida Loshaj-Shala, Toskë Kryeziu, Rrona Pozhari, Rrona Mehmeti and Fatbardha Halilaj are members of NANOALB research group.

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## THE DEFINITIONS OF INFORMATION AND SECURITY; HISTORY OF INFORMATION SECURITY DEVELOPMENT

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Taking into consideration its historical evolvement, it is evident that information security is not a new concept. Starting from the very moment of writing down the information, it presents by itself a data that can be protected, stolen, or destroyed. Throughout the whole history, without even perceiving it people had to take steps to guarantee the security of important information that they have been able to maintain. The concept of information security is quite dynamic. A behaviour that is generally accepted today can be a peril to an entity that we will work with tomorrow. Developing technology brings along the continuous innovation. Everyone handles personal information when it comes to technology development or service provision. Besides already existing services, it includes banking and other activities. Therefore, we should bear in mind that personal security cannot be ensured without guaranteeing security within each organization.

Keywords: information, information security, data carriers, coverage area, information systems, information infrastructure, computer and network security, history of information security development.

# Evaluation and comparison of two different sensors developed for the PARP inhibitor drug

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Niraparib (NPB), an inhibitor of poly adenosine diphosphate [ADP]-ribose polymerase (PARP), is utilized in the treatment of ovarian cancer resulting from BRCA mutations. In this investigation, two distinct sensor types were developed to achieve sensitive, rapid, precise, and low detection limits in the determination of niraparib [1-2]. The first is a nanosensor comprising ZnO and gold nanoparticles, determined by the direct method, while the second is a molecularly imprinted polymer-based sensor, determined by the indirect method. The development of the MIP sensor involved the use of electropolymerization on a glassy carbon electrode (GCE) with NPB serving as a template molecule, along with 3-amino phenyl boronic acid (3-APBA) and aniline (AN) as functional monomers. Both sensors were evaluated through electrochemical analyses, employing voltammetric techniques. Surface characterizations were performed using scanning electron microscopy. The nanosensor achieved a detection limit of 0.893 nM within the concentration range of 80-600 nM. The MIP sensor demonstrated lower detection limits compared to the nanosensor, with a detection limit of 0.408 pM in the concentration range of 2-10 pM. Serum applications were conducted for both sensors. The recovery results for the nanosensor ranged from 98.39% to 102.24%. For the MIP sensor, recovery results were between 100.23% and 101.08%. Both sensors yielded satisfactory recovery results. Furthermore, interference studies for both sensors were conducted to investigate the effects of common substances found in biological fluids, including K<sup>+</sup>, Na<sup>+</sup>, Ca<sup>2+</sup>, Cl<sup>-</sup>, DOP, AA, UA, and PAR.

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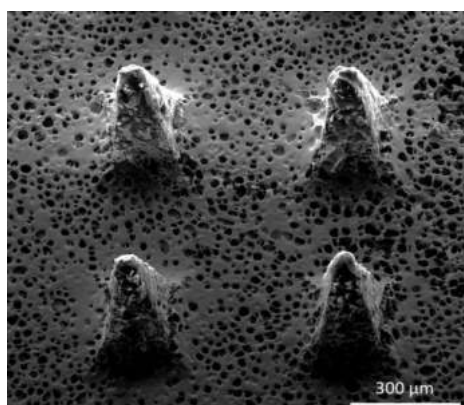
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Microneedles are micron-sized arrays arranged systematically on a small patch. They have gained prominence as a versatile technological tool with numerous applications in delivery and sensing systems, attracting increasing attention<sup>1</sup>. Microneedle-based drug delivery is an innovative technology that delivers drug compounds directly into the bloodstream through micron-sized needles<sup>2</sup>. Supermacroporous gels, known as cryogels, are unique scaffolds produced by polymerizing a monomer solution at sub-zero temperatures. These gels are widely used in various applications and have significant potential as biomaterials due to their naturally interconnected supermacroporous structures and the ease of forming composite polymers, making them superior to other porous polymer synthesis techniques<sup>3</sup>. A microneedle patch is produced using various materials, such as titanium, steel, silicon, and poly dimethylsiloxane (PDMS), through techniques like electric discharge machining, dry/wet etching, or a combination of photolithography and soft lithography. The fabricated patch is characterized by surface area measurements using the Brunauer–Emmett–Teller (BET) method, chemical composition analysis through Fourier-transform infrared (FT-IR) spectroscopy, surface morphology examination with a scanning electron microscope (SEM), 3D laser scanning microscope (Keyence VK-X100), and atomic force microscope (AFM), as well as mechanical strength assessment using dynamic mechanical analysis (DMA). A cryogel microneedle patch is produced through free radical polymerization for use as a drug delivery system. After the thawing process, the cryogel microneedle patch also undergoes characterization using SEM, FT-IR, BET, swelling tests, and gelation efficiency evaluation to determine its chemical and physical structure.

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### Figures



**Figure 1:** SEM analysis of cryogel microneedles.

**Acknowledgement:** All authors gratefully acknowledge the support from Health Institutes of Türkiye (TÜSEB) (Project Numbers: 16726).

# Synthesis, Characterization and Voltammetric Study of Dimethylammonium Lead Halide Perovskites

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Over the past decade, hybrid organic-inorganic perovskites (HOIPs) have attracted significant attention for their optoelectronic properties and potential application in photovoltaics, leading to ongoing exploration and detailed study of both new and existing HOIPs. This research focuses on the synthesis, comprehensive characterization, and cyclic voltammetric study of hybrid lead halide perovskites with the formula  $[(\text{CH}_3)_2\text{NH}_2]\text{PbX}_3$  (DMAPbX<sub>3</sub>), where X represents I<sup>-</sup>, Br<sup>-</sup>, or Cl<sup>-</sup>. A slightly modified synthesis method from literature was employed, using stoichiometric amounts of lead halides (PbX<sub>2</sub>) and dimethylammonium halides (DMAX) dissolved in acetonitrile [1] or *N,N*-dimethylformamide [2]. Controlled evaporation yielded DMAPbI<sub>3</sub> as a yellow crystalline powder, while DMAPbBr<sub>3</sub> and DMAPbCl<sub>3</sub> formed colorless hexagonal-like and needle-like crystals, respectively. X-ray powder diffraction (XRPD) confirmed distinct perovskite structures with unique lattice parameters for each halide, while scanning electron microscopy coupled with energy-dispersive X-ray spectroscopy (SEM-EDX) revealed well-defined morphologies and homogeneous elemental distribution. IR and Raman spectroscopy revealed characteristic vibrational features and reflected differences in chemical bonding and structural dynamics for each halide variant. Cyclic voltammetry (CV) studies of DMAPbX<sub>3</sub> perovskites performed in dichloromethane (DCM) with tetrabutylammonium chloride (TBAC) or tetrabutylammonium perchlorate (TBAPC) as electrolytes, using a paraffin-impregnated graphite electrode (PIGE), demonstrated significant variations in redox behavior due to different halides. The results showed that DMAPbX<sub>3</sub> perovskites are electrochemically active, with oxidation (and reduction) currents decreasing in subsequent scans, indicating partial degradation of the perovskite structure.

**Keywords:** dimethylammonium lead halide perovskites, cyclic voltammetry, XRPD, vibrational spectroscopy, SEM-EDX

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# Analysis of the Impact of Saharan Dust in the Rural Areas of Brezovica and the Concentration of PM10, PM2.5, NO2, O3, SO2, and CO

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**Abstract:** Brezovica, a well-known winter tourist destination in Kosovo, is the subject of this study. The skiing area is located on the slopes of the Sharri National Park, encompassing a territory of 39,000 hectares with alpine mountainous terrain and forests rich in flora and fauna. Although known for its clean air, warm African air masses occasionally bring Saharan dust, particularly during the spring and summer seasons.

This study analyzes standard monitoring data to assess pollution levels in an area devoid of anthropogenic factors that could degrade air quality. Parameters measured during the study include SO<sub>2</sub>, CO, NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>, expressed in µg/m<sup>3</sup>, and CO in mg/m<sup>3</sup>, based on the 2008/50/EC directive for ambient air quality and Law No. 08/L-025 for air pollution protection.

The results indicate an increase in PM<sub>10</sub> and PM<sub>2.5</sub> levels during periods when warm air masses originating from Africa or the Sahara are present.

**Keywords:** Air quality, measurement, Brezovica, winter tourism, pollution analysis, Saharan dust, air pollution, monitoring data, anthropogenic factors, PM<sub>10</sub>, PM<sub>2.5</sub>

# The impact of dust from the Sahara on PM<sub>2.5</sub> and PM<sub>10</sub> on air quality in the Pristina area

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## Abstract

The purpose of this study was to determine PM<sub>2.5</sub> and PM<sub>10</sub> dust particles in the air quality from Sahara dust in the Pristina area. The area of Pristina is the area with the most polluted air in Kosovo, due to the two power plants located in that area, the low-quality coal used as fuel by the two power plants and in households, traffic, etc. In addition to the usual state of air pollution, every year we also have very high pollution from dust coming from the Sahara, where we made a comparison of pollution from common sources and the impact of dust coming from the Sahara. PM consists of a multicomponent matrix originating from various anthropogenic sources (energy production, household, traffic, etc.) and natural sources (biomass burning, dust, etc.) which undergo several atmospheric processes.

Chronic exposure to particulate matter (PM) contributes to serious health effects, such as: accelerated aging, loss of capacity and reduced lung function, development of diseases such as asthma, emphysema, bronchitis, lung cancer and heart disease and the blows. the main causes of death.

Measurements of PM<sub>2.5</sub> and PM<sub>10</sub> dust particles for this study were made in real time for the twelve months of 2020, based on the directive 2008/50 for clean air in Europe.

The device used to measure PM<sub>2.5</sub> and PM<sub>10</sub> dust particles is the Gravimetric Optical Measure (GRIMM M180), which works according to the standard method: EN 12341:1999 and EN 14907:2005

**Key words:** air pollution, dust, power plants, coal, Pristina area.

# Identification of Targets for siRNA in Human Vena Saphena

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## Abstract

Varicose veins (VVs) can be described as tortuous and dilated palpable veins more than 3 mm in diameter. They are one of the clinical presentations of chronic venous disorder (CVD). Despite significant progress in understanding the pathogenesis of VVs, the underlying mechanisms of VVs remain incompletely elucidated.[1] Monocyte chemoattractant protein-1 (MCP-1) and its receptor CCR2 are key mediators in vascular inflammation, acting as one of the most potent chemotactic agents to monocytes.[2] In our preliminary investigations, we utilized RT-qPCR to assess TNF- $\alpha$ , VCAM, and MCP-1 gene expression levels in a subset of samples. Based on these results and supporting studies, we have decided to focus on MCP-1 for further investigation. Our study aims to investigate the expression patterns of MCP-1, in control subjects and patients with varicose veins by quantifying mRNA levels. Additionally, we will examine the correlation between blood MCP-1 concentrations and tissue-specific chemokine expression to gain insights into the systemic versus localized inflammatory response in VV patients. We tend to also investigate the potential for therapeutic intervention by using gene silencing techniques like siRNA encapsulated within exosomes to inhibit MCP-1 expression specifically. An approach that holds promise for reducing leukocyte recruitment, granting a novel strategy to mitigate the pathogenesis of inflammatory vascular diseases which include VVs. By targeting MCP-1 with siRNA, this study aims to introduce a novel molecular-based therapy for varicose veins. This could reduce inflammation and disease progression, offering a minimally invasive treatment for patients suffering from chronic venous insufficiency.

**Acknowledgments:** We express our sincere gratitude for the funding provided by the European Commission under the project titled “Nanoparticles in Environment and Medical Research” (NanoKos - 438247).

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# Integration Multi-Omics for Precision Diagnostic and Nanodelivery in Therapeutic Applications

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The integration of multi-omics approaches, including genomics, proteomics, metabolomics, and transcriptomics, will be able to develop a new era in diagnostics and personalized medicine. This study explores how multi-omics techniques can improve early diagnostic tools, identify biomarkers for noninvasive diagnostics and treatment, and connect advanced diagnostic methods with the creation of nano-delivery systems for more personalized and effective treatments. The main techniques such as paraffin embedding and microtomy for tissue preservation, Polymerase Chain Reaction (PCR) for genotyping, Western blot analysis for protein quantification, and cDNA library preparation for sequencing provide a comprehensive understanding of disease mechanisms through molecular profiling.

These techniques offer insights into the intricate interplay of genetic, protein, and environmental factors in disease mechanisms. Integration of multi-omics data with nanotechnology for optimizing nanocarrier design and further development of noninvasive nano-based methods for delivering therapeutic agents hold the promise of significantly transforming diagnostic and therapeutic landscapes, thereby enhancing patient care and outcomes in personalized medicine.

## Acknowledgments

We express our sincere gratitude for the funding provided by the European Commission under the project titled “Nanoparticles in Environment and Medical Research” (NanoKos - 438247)

**Keywords:** Multi-omics approaches, Personalized medicine, Nanotechnology, Polymerase Chain Reaction (PCR), Western blot analysis, cDNA library preparation

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# Experimental and Theoretical Insights on the adsorptive properties of Graphene Oxide toward the removal of (2E, 5E)-2,5-Bis-(2-trifluoromethyl) cyclopentanone

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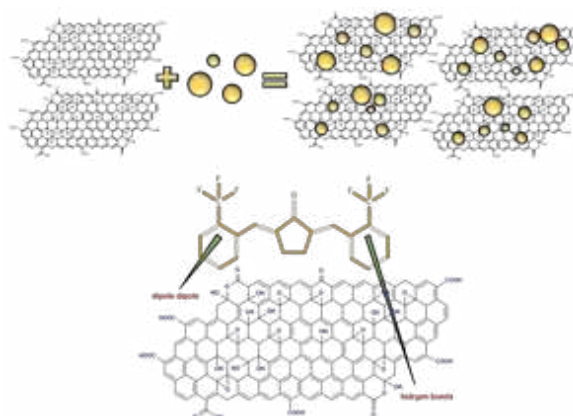
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This study focused on the adsorption of (2E,5E)-2,5-Bis-(2-trifluoromethyl)-cyclopentanone<sup>[1]</sup> using synthesized graphene oxide as an adsorbent. First, the monocarbonyl compound was synthesized<sup>[2]</sup>, and further underwent purification and structural characterization by FTIR, NMR and MS. Theoretical calculations based on Density Functional Theory (DFT) were conducted and an adsorption mechanism is proposed indicating also the interaction type and evaluating the adsorption energy<sup>[3]</sup>. Prior to its use, GOx is fully characterized by various spectroscopic methods and used as an adsorbent. The adsorption efficiency and quantity were evaluated via UV-Vis measurements. Furthermore, a comparison with a graphene as an adsorbent of choice was also performed.



*Figure 1: The interaction mechanism between GOx and the yellow color of the compound.*

Keywords: MACs; GOx; theoretical calculation; synthesis; characterization.

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# Phosphate ions detection by using an electrochemical sensor based on metal-nanoparticles modified glassy carbon electrode

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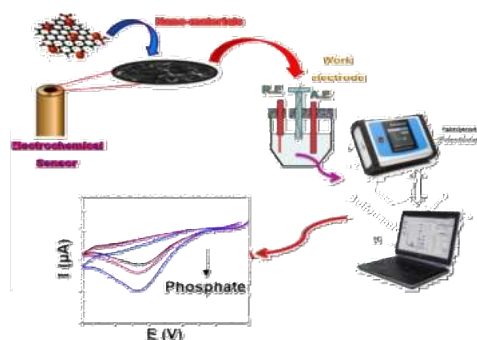
## Abstract

Phosphorus has critical values in both agricultural and biomedical applications. Determination of inorganic phosphate is of very high importance in environmental and health care applications.[1] Hence knowledge of suitable analytical techniques available for phosphate sensing for different applications becomes essential.[2] There is a need for highly sensitive, portable, inexpensive, repeatable and field deployable sensors with wide detection range to monitor the health of water and food system.[3,4] This work aims to develop electrochemical phosphate sensor based on metal nanoparticles (Au-Np) modified glassy carbon electrodes (GCE) for phosphate detection to achieve simplicity, high sensitivity, wide detection range, and high repeatability and portability. Electrochemical techniques, cyclic voltammetry and square wave voltammetry (SWV) were used to quantify the concentration of phosphate, in  $\text{NaNO}_3$   $0.5 \text{ mol/L}^{-1}$  and  $\text{KCl}$   $0.5 \text{ mol/L}^{-1}$  solution. Experimental parameters affecting the sensitivity of the nanosensors, such as amounts of the modifiers, the pH, the applied potential, and the temperature were optimized. A wide linear response for the detection of the phosphate ion was observed. The response time of the biosensors was about 5 s and maximum relative standard deviation (RSD) of around 5% confirms the repeatability of the proposed sensors. This paper suggests that nanomodified GCE sensors are promising for simple, low-cost, and portable phosphate ion detection.

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## Figures



**Figure 1:** Electrochemical determination of  $\text{PO}_4^{3-}$  with modified glassy carbon electrode



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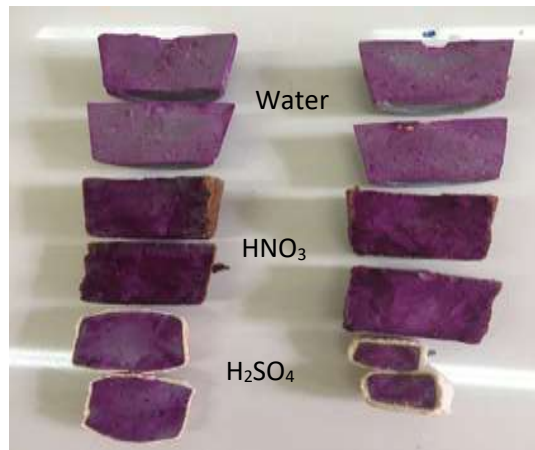
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### Abstract

Durability is an important engineering property of cement and concrete, which determines their service life. Their mechanical and physical properties may be lost due to interactions with external factors. Among different threatening factors, such as mechanical fatigue, freeze/thaw cycles, thermal stresses, chemical attack may also deteriorate the cement and concrete. Acid attack is particularly detrimental for cementitious material due to its alkaline matrix. This paper focuses on studying the durability of cement pastes from locally produced cement to ascertain their durability to withstand acidic environment degradation. Mass loss and porosity were measured after different times in aggressive solutions with different concentrations. It was concluded that the action of acid attack is dependent on the type of acid, acid concentration, w/c ratio and exposure time. The degradation was significant in long periods of contact time and higher concentrations of acid. Immersion in sulphuric acid leads to stronger attack for the studied samples.

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**Figure 1.** Acidic degradation of cement pastes, 3% acid concentration (left) and 5% acid concentration (right)

# Genetic analysis of VEGF gene polymorphisms in women with recurrent pregnancy loss; development of a SNaPshot genotyping technique.

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Vascular Endothelial Growth Factor A (VEGF gene) has significant role in angiogenesis and recently studies suggest evidence for its implications in embryo development and critical role in fetal and placental angiogenesis where formation of vascular anomalies contribute to recurrent pregnancy loss (RPL). Here we designed a multiplex single-base extension method SNaPshot for identification of variants within the *VEGF* gene among a group of women experiencing recurrent early pregnancy loss. All individuals were analyzed for the presence variants in the *VEGF* gene using a multiplex SNaPshot kit for the reaction followed by capillary electrophoresis on a SeqStudio Genetic Analyzer (Applied Biosystems). Of the total of 91 women, 48 with pregnancy losses and 43 controls, 41 had more than two pregnancy losses. We excluded the cause of miscarriage by aneuploidy in the POCs (trisomi 13, 18, 21, X,Y). Two variants in the *VEGF* gene respectively (c.-1154G/A (rs1570360) and c.\*237C/T (rs3025039) were identified and their presence observed in higher prevalence of the heterozygous and mutant homozygous genotypes for the both *VEGF* variants in group of women experienced RPLs compared with controls. All the variants of VEGF gene play a role in an increased frequency of RPL, however c.\*237C/T genotypes seems to affect the embryo development and placental angiogenesis. By optimizing this technique, we can develop improved protocol and adding biomarkers in monitoring pregnancy outcome.

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# Development of Lipid-Based Mucoadhesive Drug Delivery Systems by Thiolation of Non-Ionic Surfactants

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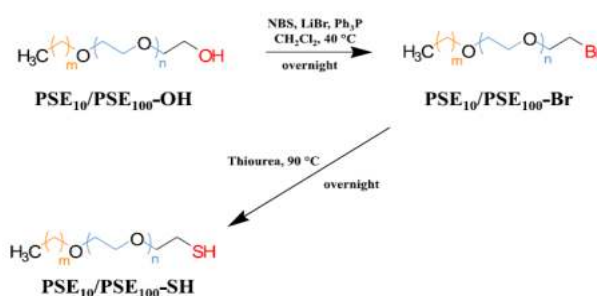
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## Abstract

Drug administration via mucosal membranes is preferred over other routes, due to higher patient compliance and acceptance. To address challenges like poor drug solubility and low bioavailability, lipid-based formulations such as self-emulsifying drug delivery systems (SEDDS) and nanostructured lipid carriers (NLCs) have been developed. Among these, SEDDS stand out for their ease of production and scalability in manufacturing [1]. Furthermore, in comparison to solid lipid nanoparticles, liquid lipid inside NLCs improves the loading capacity for drugs and causes a stable incorporation of them inside the carrier [2]. A potential approach to address the short residence time in the GIT is to functionalize the surface of these nanocarriers with thiol groups, thereby enhancing their mucoadhesive properties [3]. One common method to prepare thiolated nanocarriers is the coating of already formed nanocarriers with thiolated excipients [4]. This study aimed to enhance the benefits of PEGylated nanocarriers by developing SEDDS and NLCs containing thiolated PEGylated surfactants, designed to create nanocarriers with strong mucoadhesive properties. To achieve this, surfactants with both short and long PEG chains (Fig. 1) were selected because the length of the PEG chain can impact its conformation and its behavior in biological systems. Polyoxyethylene (10) stearyl ether and polyoxyethylene (100) stearyl ether were thiolated for the first time by substituting the terminal hydroxyl group with a thiol group. The thiolated surfactants were characterized by FT-IR, NMR and Ellman's test. All nanocarriers had a size <250 nm, a maximum PDI of 0.3 and a  $\zeta$  potential < -9.0 mV. The mucoadhesive properties and increase in viscosity of SEDDS and NLCs ranked: PSE<sub>100</sub>-OH < PSE<sub>10</sub>-OH < PSE<sub>100</sub>-SH < PSE<sub>10</sub>-SH. All formulations of these drug delivery systems have been tested in mucosal permeability models, developed in our laboratory. The short chain PSE<sub>10</sub>-SH showed higher mucus interactions than the long chain PSE<sub>100</sub>-SH for both SEDDS and NLCs.



**Figure 1.** Synthetic pathway for the preparation of thiolated surfactants

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# Lignin Modified Electrodes Developed for Biosensing of DNA Interaction with Mitomycin C

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## Abstract

Lignin is the second most abundant biopolymer after cellulose in biomass with a polyphenolic structure [1]. Many studies have been carried out in recent years for the use of lignin in many areas, such as gene delivery, drug encapsulation, tissue engineering, biological imaging, and biosensors [2]. Electrochemical biosensors are frequently used to detect specific biomolecules, DNA hybridizations, and drug-DNA interactions due to their advantages, such as high sensitivity and low detection limit [3,4]. Elucidation of drug-DNA interactions is very important, especially in pharmaceutical development processes [4]. For this reason, the study of the interactions of anticancer drugs with DNA has been a subject of interest in recent years [5,6]. Mitomycin C (MC), an antitumor antibiotic, is one of the major drugs used in the treatment of cancer. MC is used in the treatment of many types of cancer, especially breast, bladder, stomach, and oesophageal cancer [7]. In this study, lignin modified electrodes were first developed, and then their application to biosensing of interaction between DNA and MC was explored. The electrochemical behavior of lignin-modified electrodes was investigated by cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS) techniques. Experimental conditions were optimized in different concentrations of lignin and also in MC interaction times. Electrochemical detection of interaction between DNA and MC was explored.

**Acknowledgements:** Arzum Erdem Gürsan would like to express her gratitude to the Turkish Academy of Sciences (TÜBA) as a Principal member for its partial support.

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Metal organic frameworks (MOFs) have potential for being applied as enhanced labels on sensors and biosensors. In our approach, we combine magnetic nanobeads (MNBs) as the core material and defective MOFs as the shell to fabricate a nanohybrid with highly tunable structures of large surface areas, well-defined porosity and chemical stability.

MOFs have been reported in diverse sensing applications, such as gas adsorption[1], catalysis[2], drug delivery[3], and biosensing (e.g. lateral flow tests)[4].

Our nanohybrid could work as a probe for detecting glycoproteins, present in several bacteria, by combining boronic acid on their surface. In this way, the nanohybrid would be able to recognize bacteria without using antibodies, being thus more stable and cheaper to produce. In addition, MOFs could act as a fluorescent label, while taking advantage of the magnetic properties of MNBs to pre-concentrate and extract the targets from complex samples..

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# Novel Approaches in Headache Management: Beyond Traditional NSAIDs with Indomethacin and Innovative Drug Delivery

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**Background:** Headache disorders such as hemicrania continua (HC) and paroxysmal hemicrania (PH) pose unique treatment challenges, as they are unresponsive to most NSAIDs. Indomethacin is highly effective in treating these conditions, positioning it as the cornerstone of their management. However, the limitations of traditional NSAID therapies, such as gastrointestinal side effects, have spurred interest in novel drug delivery systems to enhance therapeutic outcomes.

**Objective:** This study investigates indomethacin's role in managing HC and PH, while exploring cutting-edge drug delivery technologies, particularly solid lipid nanoparticles and polymeric nanoparticles. The focus is on improving indomethacin's pharmacokinetics, minimizing side effects, and increasing precision in targeting headache-related pathways.

**Methods:** A systematic review of clinical and experimental studies from the past decade was conducted. Key areas of investigation include indomethacin's pharmacodynamic properties, its mechanisms in headache disorders, and the potential of nanoparticle-based systems to enhance its bioavailability and therapeutic effect.

**Results:** Indomethacin not only inhibits COX enzymes but also impacts neurovascular processes critical to the pathophysiology of HC and PH. Emerging research on nanotechnology-based delivery, particularly through solid lipid and polymeric nanoparticles, shows promise in reducing systemic adverse effects and providing more efficient CNS targeting of indomethacin, which could improve its efficacy in headache management.

**Conclusion:** While indomethacin remains a critical treatment for indomethacin-responsive headaches, integrating nanotechnology-based delivery methods such as solid lipid and polymeric nanoparticles could further enhance its therapeutic profile. These innovations hold the potential to reduce side effects and optimize drug delivery in the central nervous system, expanding indomethacin's role in managing headache disorders.

## **Nano-Enhanced Flavonoids: Transforming Diabetes Treatment**

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Diabetes, a chronic metabolic disorder, continues to affect millions worldwide, necessitating the development of innovative therapeutic approaches. Flavonoids, naturally occurring compounds found in fruits, vegetables, and plants, have shown promising potential in managing diabetes due to their antioxidant, anti-inflammatory, and insulin-sensitizing properties. However, the clinical application of flavonoids is often limited by poor solubility, bioavailability, and rapid metabolism.

Nanotechnology offers a transformative solution by enhancing the therapeutic efficacy of flavonoids in diabetes treatment. By encapsulating flavonoids within nanocarriers such as liposomes, nanoparticles, and polymeric micelles, it is possible to improve their stability, solubility, and controlled release, leading to better absorption and prolonged therapeutic action. These nanoformulations can also facilitate targeted delivery to pancreatic beta cells and tissues affected by diabetes, potentially reducing side effects and improving patient outcomes.

This emerging intersection of nanotechnology and flavonoid-based therapies represents a promising frontier in diabetes management, offering a novel approach to enhance the bioactivity of flavonoids and provide more effective, long-lasting treatments for patients.

# Per- and Polyfluoroalkyl Substances (PFAS) in the Environment: An Overview of Three Case Studies

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## Abstract

Per- and polyfluoroalkyl substances (PFAS), known as “forever chemicals,” are used in a wide range of consumer and industrial products, including non-stick cookware, leather coatings, cleaners, shampoos, pesticides, firefighting foam, and many others [1]. Due to their persistence and bioaccumulation, PFAS are found in air, water, soil, and food. PFAS have been associated with kidney and testicular cancers, as well as several other adverse health effects in humans, including dyslipidemia, hormonal imbalance, immunotoxicity, and kidney injury [2]. Detecting and monitoring PFAS with environmental Nanosensors can facilitate rapid detection, reduce costs, and inform prevention strategies. This presentation will share three different case studies related to PFAS and environmental health concerns.

**Case Study 1:** PFAS are widely used in construction coatings and painting products. Occupational exposure as a painter has been classified by the International Agency for Research on Cancer (IARC) as a Group 1 carcinogen [3]. Exposure to PFAS has emerged as a significant concern and a possible contributing factor to the high risk of cancer among painters. We will present the results of a preliminary study on PFAS body burden among construction painters and product characterization. Independent chemical analyses are needed to determine specific PFAS compounds and their concentrations in products used by construction workers to guide targeted PFAS biomonitoring and prevention efforts.

**Case Study 2:** PFAS are the primary ingredient in Aqueous Film Forming Foams (AFFF) used to suppress Class B fires. The firefighting profession recently has been categorized as a Group 1 carcinogen. We will discuss the results of a national survey of fire training facilities (FTFs) aimed at collecting information on the current state of firefighter foam use, best practices, barriers, lessons learned from current efforts to transition to fluorine-free foams (FFFs), and field experiences using these alternatives [4]. Further testing is needed to evaluate these new alternatives as PFAS-free products.

**Case Study 3:** Funded by the Research Expertise from the Academic Diaspora Fellowship (READ) program in collaboration with our colleagues in Tirana, we measured PFAS concentrations in irrigation waters in Albania to determine contamination hotspots. Water samples from surface waters (e.g., rivers, streams, and reservoirs) and groundwater systems (e.g., wells) in Albania were analyzed for 50 PFAS at UMass Lowell. This presentation will cover our preliminary findings and suggestions for next steps.

Through this presentation, we aim to alert the NANOBalkan conference audience to the urgent need for developing environmental Nanosensors to detect PFAS sources, measure hotspot pollution, and identify communities at high risk.

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