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Doctoral Thesis

Bioactive and Nanostructured Hydrogels for Personalized Bone Regeneration

- Extended Abstract -

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Summary

1. Context and theoretical framework

1.1. Introduction

Critical-size bone defects represent a major challenge in orthopedic practice and reconstructive surgery, exceeding the natural regenerative capacity of bone tissue. Their **etiology** is diverse, including severe trauma, bone tumor resections, congenital malformations, or degenerative conditions such as osteonecrosis. In the absence of effective tratment solutions, these lesions lead to the **loss of functionality of the affected bone segment**, limited mobility, and a decreased quality of life for patients. Beyond the complex clinical and therapeutic challenges, the management of bone defects generates a significant socio-economic impact on healthcare systems [2].

Conventional therapeutic approaches present significant limitations. Autografts, though widely used for their osteogenic, osteoconductive, and osteoinductive properties, are constrained by donor site morbidity, reduced tissue availability, prolonged operative time, and possible surgical complications, resulting in increased patient discomfort [3]. Allografts may elicit immunological or infectious reactions, while xenografts often demonstrate poor integration and could trigger foreign body responses. Consequently, long-term performance remains suboptimal, particularly for anatomically complex defects or compromised biological environments.

Thus, for critical-size bone defects, defined as the **smallest defects that cannot be repaired through natural bone regeneration**, surgical intervention and the use of biomaterial-based structures are indispensable for restoring the structural and functional integrity of the affected area [4].

In this context, **bone tissue engineering (BTE)** provides a promising alternative through the development of **bioactive scaffolds** which can be loaded with cells and biochemical factors that are capable to guide tissue regeneration. Such a construct intended for bone regeneration must simultaneously meet complex requirements: to provide adequate mechanical support, exhibit high porosity and hydration to allow cell migration and vascularization, and deliver the biological signals required for osteogenesis and tissue remodeling. Ideally, these structures should provide structural stability, guide osteogenic cell

differentiation, promote vascularization, and degrade at a rate synchronized with the formation of new bone tissue.

The complexity of bone defects and the wide range of clinical scenarios require the development of bespoke patient solutions. In cases such as craniofacial reconstruction, segmental defects following tumor resections, or femoral head osteonecrosis, standardized implants fail to provide satisfactory anatomical and functional restoration.

Advances in medical imaging, three-dimensional modeling, and additive manufacturing technologies have made it possible to design and produce customized implants. The advantages of personalized BTE implants, tailored to the shape and size of the defect, include reducing the need for intraoperative adjustments (such as the removal of healthy bone tissue to ensure compatibility of the affected area with the geometry of a standard metallic implant), reducing operative time and limiting blood loss, while lowering the risk of complications, and enhancing biological integration [5, 6].

1.2. Hydrogels used in bone regeneration

Hydrogels are among the most extensively studied classes of biomaterials for regenerative applications, owing to their structural and functional resemblance to the natural extracellular matrix (ECM). They consist of three-dimensional polymer networks capable of retaining large amounts of water, thereby ensuring permeability for nutrients and metabolites and creating a microenvironment that could support cell adhesion and proliferation.

By adjusting their crosslinking degree and composition, the mechanical properties, degradation rate and stability, hydrogels can be tailored for specific applications. Nevertheless, simple hydrogels lack sufficient mechanical strength for large bone defects or for those in regions exposed to significant mechanical loads, and they also display limited osteoinductive capacity. This underscores the need for solutions based on **nanostructural reinforcement** and **functionalization with bioactive agents**, integrating structural advantages with the desired biological effects to generate effective constructs for bone tissue regeneration.

Based on the aforementioned properties and their compatibility with modern processing techniques, several polymers have been identified as promising base materials for bone regeneration, including **methacrylated gelatin (GelMA), alginate (Alg)**, and **gellan gum (GG).** These polymers were selected for their biocompatibility, adjustable gelation behavior, and adaptability to advanced fabrication methods such as casting, extrusion-based 3D printing, and bioprinting.

- **GelMA**

GelMA is a photocrosslinkable derivative of gelatin that preserves bioactive sequences promoting cell adhesion and enables the tuning of mechanical properties through control of the methacrylation degree and photopolymerization conditions. It is biocompatible, biodegradable, and suitable for bioprinting.

However, in concentrations that support cell viability, GelMA hydrogels display limited mechanical strength and inadequate osteoinductive capacity, highlighting the need for functionalization with additional compounds.

- **Alg**

Alg is a natural polysaccharide extracted from brown algae, widely used due to its ability to form stable gels through ionic crosslinking in the presence of divalent ions, especially Ca^{2+}. It is highly biocompatible, easy to process, and frequently used in printing applications. In its native form, alginate is distinguished by its bioinert character, which limits its interactions with cells. In this regard, it is often chemically functionalized or combined with other natural polymers or bioactive compounds to promote cell adhesion and differentiation.

- **GG**

GG is an anionic polysaccharide used to produce stable hydrogels through simple ionic gelation. Its stable three-dimensional network and favorable rheological properties make it suitable for injectable applications as well as extrusion-based processing. However, similar to Alg, the lack of bioactive groups requires GG to be combined with nanoparticles, bioactive compounds, or osteoinductive molecules in order to enhance its biological functionality.

1.3. Nanoparticles and bioactive compounds for hydrogel functionalization

Integrating nanoparticles and bioactive compounds into polymeric matrices is a strategic approach in designing multifunctional hydrogels for bone regeneration. This strategy can enhance the mechanical performance of the hydrogels, while inducing targeted biological responses, resulting in hybrid platforms with strong potential to support bone regeneration.

Within the framework of this thesis, several strategies were investigated to enhance the performance of biomaterial constructs for bone tissue regeneration. **Diamond nanoparticles (NDs)** and **magnesium-doped nanohydroxyapatite (MgHA)** primarily served as structural reinforcement agents and enhancers of osteoconductivity, whereas natural bioactive molecules,

including **Aloe vera (AV)** extracts and **icariin (ICA)**, contributed through their osteoinductive, antioxidant, and antibacterial properties.

- **NDs**

ND are carbon-based nanoparticles with a functionalizable surface rich in chemical groups, able to enhance mechanical properties and facilitate initial cell interactions. When embedded in hydrogel matrices, they can form high-stiffness islands that act as nanolocalized reinforcement agents.

By generating such stiff microdomains within otherwise soft hydrogels, ND trigger cytoskeletal reorganization and transmit mechanotransduction signals, which stimulate osteogenic differentiation and promote mineralized matrix deposition, essential for applications in bone regeneration [7].

- **MgHA**

MgHA is a bioactive bioceramic with both osteoconductive and osteoinductive roles, capable of releasing Mg^{2+} ions that play a key role in mineralization process. As an advanced form of modified nanohydroxyapatite, MgHA exhibits enhanced osteoinductive and osteoconductive properties, controllable resorption, and physicochemical characteristics favorable for its incorporation into hydrogels or 3D bioprinting systems. In addition, complementary to its biological activity, MgHA can contribute to improving the mechanical properties of hydrogels [8].

- **Bioactive compounds from AV**

AV is a medicinal plant that has been used for thousands of years for its anti-inflammatory, antioxidant, and regenerative properties, due to its complex content of polysaccharides, amino acids, vitamins, and phenolic compounds [9]. The bioactive compounds are primarily concentrated in the gel of mature AV leaves, where the polysaccharide acemannan (ACE) is predominant and has been associated with many of the plant's reported therapeutic effects. However, the beneficial effects observed in bone regeneration arise from a complex synergism of the entire AV extract, which can modulate cell proliferation and differentiation, regulate the inflammatory response, and promote extracellular matrix (ECM) formation simultaneously [10].

In addition to their osteogenic effects, AV extracts play a key role in modulating immune and inflammatory processes by reducing the secretion of specific cytokines and regulating macrophage activity, thereby supporting bone healing [11]. Moreover, the components of the AV extract can influence the physicochemical properties of hydrogel-based composites in which they are incorporated, enhancing water adsorption and retention capacity while also improving permeability [10]. These features facilitate efficient nutrient diffusion through the hydrogel network and help maintain cell viability.

- **ICA**

ICA is a natural bioflavonoid known for its osteogenic and angiogenic effects, traditionally used in Chinese medicine to treat osteoporosis. It was shown to promote osteoblast differentiation, while inhibiting osteoclast differentiation and activity by downregulating the expression of bone resorption markers [12]. Moreover, ICA promotes angiogenesis by enhancing the migration, proliferation, and organization of endothelial cells into capillary structures, thereby supporting new blood vessel formation [13].

Incorporating ICA into hydrogels and 3D-printed composites enables the controled release of ICA, providing osteoinductive properties to scaffolds that are comparable to those of bone morphogenetic protein 2 (BMP-2) in stimulating mineralization and the expression of osteogenic markers [14].

1.4. Reinforcing hydrogels using nanofibrillar components

Beyond the integration of inorganic nanoparticles and natural bioactive compounds, another research strategy focuses on reinforcing polymeric matrices by embedding nanofibrillar components. This approach is based on the structural analogy with native bone ECM, characterized by a complex architecture of mineralized collagen fibers, that provides both mechanical strength and essential biological signaling.

Polymeric or biopolymeric fibrillar nanostructures can simultaneously improve mechanical stability, porosity control, and the transmission of mechanotransduction signals when embedded within hydrogel matrices [15]. Their orientation and organization can further direct cell migration and promote ECM deposition, two critical processes for bone tissue regeneration [16].

In this thesis, two nanofibrillar reinforcement strategies were explored: incorporating cellulose nanofibrils to produce homogeneous composites with enhanced mechanical and

rheological properties, and integrating micro- and nanofibrillar structures fabricated through melt electrowriting (MEW).

- **Reinforcement through Incorporation of Cellulose Nanofibrils (CNF)**

Cellulose nanofibrils (CNFs) have attracted considerable interest as nanostructured reinforcement agents due to their high aspect ratio, large specific surface area, and inherent biocompatibility and biodegradability [17]. TEMPO-mediated oxidation enhances the dispersibility and colloidal stability of CNFs by introducing carboxyl groups, resulting in thinner, more individualized fibrils (TO-CNFs) [18]. These fibrils form porous, hydrophilic networks resembling the ECM, which promote cell adhesion and differentiation, making them highly applicable to bone regeneration.

Furthermore, CNFs exhibit high mechanical strength due to their dense network of hydrogen bond-forming groups, along with rheological properties such as shear-thinning and thixotropy, particularly valuable features for 3D (bio)printing. Fibril alignment during extrusion enhances construct integrity, while TEMPO oxidation reduces friction and enables low-pressure extrusion, preserving biological components. Consequently, incorporating CNFs into hydrogel matrices is an effective strategy for producing composites with superior mechanical and bioactive properties.

- **Reinforcement through incorporation of micro- and nanofibrillar elements fabricated by MEW**

MEW is a high-resolution additive manufacturing technology capable of producing micro- and nanoscale fibers with precise deposition according to predefined patterns. By enabling the architectural control of scaffolds, MEW elements directly shape cellular responses, as fiber orientation influences cell morphology and intracellular mechanical signaling [19]. The process relies on parameters such as polymer molecular weight, electrical conductivity, applied voltage, extrusion pressure, and needle-collector distance. Polycaprolactone (PCL) is most widely used material for MEW due to its excellent processability, stable thermal behavior, low cost, and clinical approval, while also exhibiting a slow degradation rate of 2-4 years [20].

Embedding fibrillar networks with precisely defined architectures produced by MEW into soft hydrogel matrices results in composites with increased stiffness. Visser et al. [21] demonstrated this by infiltrating a GelMA hydrogel into an ordered PCL microfiber network, which significantly increased stiffness compared to the hydrogel alone. Thus, by enabling fine

control over fiber diameter and network architecture, MEW makes it possible to design fibrous structures that effectively reinforce hydrogels, imparting superior stiffness and stability while influencing cellular mechanobiology and tissue regeneration processes.

Building on these theoretical foundations and the limitations identified in the literature, this thesis aimed to develop and investigate integrated experimental strategies for designing and characterizing nanostructured composite hydrogels tailored for personalized bone regeneration.

2. General and specific objectives

The general objective of this thesis consisted in the **design, development, and characterization of nanostructured composite hydrogels** with optimized mechanical and biological properties, capable of supporting bespoke bone regeneration. To achieve this, the research was organized into four complementary directions, each aimed at developing innovative strategies for the reinforcement and functionalization of hydrogel matrices.

The first research direction focused on developing **GelMA-based hydrogels functionalized with bioactive extracts from AV**. The objective was to examine the role of AV polysaccharides in polymer network formation, as well as in shaping the rheological and antibacterial properties, to validate the potential of these formulations as biomaterials with enhanced functionality.

The second research direction was centered on **integrating fibrillar structures fabricated via MEW into thin hydrogels**, producing hybrid composites with controlled architecture and enhanced mechanical strength. These systems were specifically designed for applications in **the reconstruction of osteonecrotic surfaces**, where simple hydrogels are unable to provide adequate support.

The third research direction aimed at developing **GG-based scaffolds reinforced with ND and bioactivated with ICA.** This combination enabled the investigation of complementary effects between the mechanical reinforcement provided by ND and the biological stimulation induced by ICA, with the focus of creating structures with enhanced functional and biological performance.

The fourth research direction involved **developing multicomponent formulations composed of GelMA, TO-CNF, and Alg, enriched with ND and MgHA**. The goal was to

produce bioinks suitable for 3D bioprinting that combine printability and stability with the capacity to induce relevant osteogenic responses.

Through the convergence of these directions, the thesis aimed to validate complementary strategies involving functionalization with natural bioactive molecules, the integration of nanoparticles, and reinforcement elements, with the goal of **developing multiscale hybrid systems that are both processable and osteoinductive, designed for applications in personalized bone regeneration.**

3. Original contributions

The original contributions of this doctoral thesis fall within the field of polymeric biomaterials for bone regeneration and propose four complementary research directions. These directions explore distinct strategies for hydrogel functionalization and reinforcement, aiming to develop composite systems that successfully integrate processability, structural stability, and biological stimulation.

The first research contribution involved developing hydrogels based on methacrylated gelatin functionalized with compounds extracted from *Aloe Vera Barbadensis Miller*. The originality of this research direction lies in the use of a complex natural extract, rich in ACE and other bioactive compounds, which enabled the creation of materials with enhanced properties. Compositional analysis confirmed the presence of ACE and other bioactive compounds within the hydrogel structure, while their integration into the polymer network led to modified rheological properties and increased hydration capacity. Moreover, the formulations displayed antibacterial activity against *Escherichia coli*, demonstrating the possibility of producing multifunctional biomaterials that combine structural features with enhanced biological effects. This study validated a natural functionalization strategy that adds biological value to a well-established polymeric matrix.

The results of this study were published during the doctoral program and are available in the article: Carmen-Valentina Nicolae, Iulia-Maria Iordache, Adela Banciu, Izabela-Cristina Stancu, ***Aloe Vera-loaded gelatin methacryloyl hydrogels as potential bone biomaterials***, published in U.P.B. Sci. Bull., Series B, Vol. 86, Iss. 4, 2024, ISSN 1454-2331, WOS:001380943500010,https://old.scientificbulletin.upb.ro/rev_docs_arhiva/full116_952338.pdf, IF_{2024}=0.3, Q4.

This work was supported from the project *Integrating mechanically-tunable 3D printing with new bioactive multi(nano)materials for next functional personalized bone regenerative scaffolds*, PN-III-P4-PCE-2021–1240, no. PCE 88/2022.

The second research contribution focused on the integration of MEW-fabricated structures into thin hydrogels to obtain hybrid composites with controlled architecture and superior mechanical stability. The novelty lies in the use of PCL meshes produced under parameters optimized through Design of Experiments for high instabilities that produce wide multifibrillar strands for improved contact between the MEW structure and the hydrogel, followed by enhancing the hydrogel-polymer interface by plasma-treating the fibrillar elements, which enabled the consolidation of interactions between the two phases. The results demonstrated that integrating MEW networks led to a significant increase in the stiffness of thin hydrogels, opening possibilities for the application of these systems in the regeneration of osteonecrotic surfaces.

The results of this study were published during the doctoral program and are available in the article: Carmen-Valentina Nicolae, Elena Olăreț, Adriana-Elena Bratu, Adriana Lungu, Izabela Cristina Stancu, Bogdan Stelian Mastalier Manolescu, **Reinforcing melt electrowritten elements with entangled multifibrillar strands for thin hydrogels with potential in bone resurfacing**, *Materials & Design (Elsevier)*, Volume 237, 2024, 112545, ISSN 0264-1275, WOS:001138868400001, https://doi.org/10.1016/j.matdes.2023.112545, IF_{2024}=7.9, Q1.

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A treia contribuție a constat în dezvoltarea de scaffolduri pe bază de GG ranforsate cu ND și bioactivate cu ICA. Originalitatea acestei direcții derivă din asocierea între ranforsarea nanostructurală localizată și bioactivarea naturală, două strategii rar investigate concomitent în literatura de specialitate. Experimentele au evidențiat faptul că un conținut redus de ND este suficient pentru a îmbunătăți proprietățile mecanice și nanomecanice ale scaffoldurilor, iar adsorbția ICA pe suprafața ND a condus la o stimulare osteogenă pronunțată, cu depunerea de ECM mineralizată. Prin corelarea proprietăților nanomecanice și răspunsului celular, această

direcție aduce o contribuție originală la înțelegerea modului în care nanoparticulele și moleculele bioactive pot acționa complementar pentru a genera sisteme eficiente în regenerarea osoasă.

The results of this study were published in full during the doctoral program and are available in the article: Carmen-Valentina Nicolae, Masoumeh Jahani Kadousaraei, Elena Olăreț, Andrada Serafim, Mehmet Serhat Aydin, Ioana-Teodora Bogdan, Adriana Elena Bratu, Raluca-Elena Ginghină, Alexandra Dobranici, Sorina Dinescu, Kamal Mustafa, Izabela-Cristina Stancu, **Enhancing cellular interactions through bioactivation and local nanomechanical reinforcement in nanodiamond-loaded 3D printed gellan gum scaffolds**, *Materials (MDPI)*, in the special issue *Engineering the Future: Advances in 3D Printing Formulations for Biomedical Solutions*, 2025, WOS:001569946100001, https://doi.org/10.3390/ma18174131, IF_{2024}=3.2, Q2.

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The fourth contribution focused on the development of multicomponent bioinks based on GelMA, TO-CNFs, and Alg, functionalized with ND and MgHA, designed for the bioprinting of constructs with osteoinductive properties. The novelty of this contribution lies in the complexity of the developed formulations, the multiscale characterization of those systems that combine favorable rheological properties (shear-thinning, thixotropy) with structural stability and enhanced bioactivity. Bioprinting enabled the fabrication of structures with high geometric fidelity and interconnected porosity, while biological tests demonstrated that the dual inclusion of ND and MgHA had complementary effects on cell proliferation and on the expression of osteogenic markers in encapsulated MG-63 cells. Thus, the research provides an original contribution toward validating multicomponent bioinks with real potential for personalized clinical applications.

The results of this study were published in full during the doctoral program and are available in the article: Carmen-Valentina Nicolae, Masoumeh Jahani Kadousaraei, Shuntaro Yamada, Mehmet Serhat Aydin, Niyaz Al-Sharabi, Elisabetta Campodoni, Monica Sandri, Doris Steinmüller-Nethl, Kristin Syverud, Bogdan Ștefan Vasile, Ahmad Rashad, Izabela-Cristina Stancu, Kamal Mustafa, **Nanostructured Multicomponent Bioinks with Nanodiamond and Magnesium-Doped Nanohydroxyapatite for Enhanced Bone Tissue**

Engineering, published in *Materials & Design (Elsevier)*, https://doi.org/10.1016/j.matdes.2026.115510, IF_{2024}=7.9, Q1.

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Overall, these contributions demonstrate that the integration of natural bioactive compounds, nanoparticles, and fibrillar structures obtained through advanced manufacturing technologies constitutes an original strategy for the development of composite hydrogels as platforms to support bone regeneration. The thesis demnostrates that multiscale approaches can harmonize processability, mechanical stability, and the induction of favorable biological responses, producing hydrogel systems with enhanced properties compared to conventional hydrogels. The findings validate the proposed hypotheses and open promising perspectives for clinical translation in the personalized treatment of complex bone defects.

4. General conclusions

The research conducted within this doctoral thesis demonstrated the feasibility of developing composite and nanostructured hydrogel systems, processable through modern manufacturing techniques, and capable of addressing the complex requirements of personalized bone regeneration. Through complementary approaches integrating functionalization with natural compounds, integration of inorganic and carbon-based nanoparticles, and architectural reinforcement using additively fabricated fibrillar structures, hybrid biomaterials with superior structural, mechanical, and biological properties were obtained. The results confirm the added value of these strategies and highlight their potential for translation into clinical applications, particularly in the treatment of critical bone defects where conventional solutions remain insufficient.

The thesis advanced the field of tissue engineering by providing robust experimental evidence for the efficiency of multiscale hybrid systems capable of integrating processability and structural stability with the stimulation of osteogenesis-specific biological responses. At the same time, the research directions explored outline new perspectives for extending investigations toward preclinical and clinical models, as well as for adapting the developed strategies to other tissue types or complex regenerative applications. Collectively, the findings highlight the role of composite hydrogels and advanced manufacturing technologies in the transition toward personalized bone regeneration.

5. Dissemination

Publications included in this thesis:

1. **Carmen-Valentina Nicolae**, Iulia-Maria Iordache, Adela Banciu, Izabela-Cristina Stancu, **Aloe Vera-loaded gelatin methacryloyl hydrogels as potential bone biomaterials**, *U.P.B. Sci. Bull., Series B*, Vol. 86, Iss. 4, 2024, ISSN 1454-2331, https://old.scientificbulletin.upb.ro/rev_docs_arhiva/full116_952338.pdf, **IF2024 = 0.3, Q4.**
2. **Carmen-Valentina Nicolae**, Elena Olăreț, Adriana-Elena Bratu, Adriana Lungu, Izabela-Cristina Stancu, Bogdan Stelian Mastalier Manolescu, **Reinforcing melt electrowritten elements with entangled multifibrillar strands for thin hydrogels with potential in bone resurfacing**, *Materials & Design (Elsevier)*, Vol. 237, 2024, 112545, ISSN 0264-1275, https://doi.org/10.1016/j.matdes.2023.112545, **IF2024 = 7.9, Q1.**
3. **Carmen-Valentina Nicolae**, Masoumeh Jahani Kadousaraei, Elena Olăreț, Andrada Serafim, Mehmet Serhat Aydin, Ioana-Teodora Bogdan, Adriana Elena Bratu, Raluca-Elena Ginghină, Alexandra Dobranici, Sorina Dinescu, Kamal Mustafa, Izabela-Cristina Stancu, **Enhancing cellular interactions through bioactivation and local nanomechanical reinforcement in nanodiamond-loaded 3D printed gellan gum scaffolds**, *Materials (MDPI)*, *18*(17), 2025, 4131, special number *Engineering the Future: Advances in 3D Printing Formulations for Biomedical Solutions,* https://doi.org/10.3390/ma18174131, **IF2024 = 3.2, Q2**.
4. **Carmen-Valentina Nicolae**, Masoumeh Jahani Kadousaraei, Shuntaro Yamada, Mehmet Serhat Aydin, Niyaz Al-Sharabi, Elisabetta Campodoni, Monica Sandri, Doris Steinmüller-Nethl, Kristin Syverud, Bogdan Ștefan Vasile, Ahmad Rashad, Izabela-Cristina Stancu, Kamal Mustafa, **Nanostructured multicomponent bioinks with nanodiamond and magnesium-doped nanohydroxyapatite for enhanced bone tissue engineering,** *Materials & Design (Elsevier)***,** Vol. 262, 2026, 115510, ISSN 0264-1275, https://doi.org/10.1016/j.matdes.2026.115510**, IF2024 = 7.9, Q1.**

Conferences:

1. **Melt Electrowritten Scaffolds as Reinforcing Elements for Bone Surface Reconstruction**, **Carmen-Valentina Nicolae**, Elena Olaret, Izabela-Cristina Stancu - RICCCE 2022 - 22nd Romanian International Conference on Chemistry and Chemical Engineering, Sinaia, Romania, 7-9 September 2022 - **oral presentation**, **Professor Sorin Roșca Award in the short presentation competition for young researchers.**

2. **Melt Electrowritten Scaffolds as Reinforcing Elements for Bone Surface Reconstruction**, Carmen-Valentina Nicolae, Elena Olaret, Izabela-Cristina Stancu - *EmergeMAT, 5th International*

Conference on Emerging Technologies in Materials Engineering, 20-21 October 2022, Bucharest, Romania - **poster presentation**.

3. **Bone Surface Reconstruction Using Melt Electrowritten Reinforced Thin Scaffolds**, Carmen-Valentina Nicolae, Elena Olaret, Izabela-Cristina Stancu - *BEHEALTH - International Online Event in Healthcare*, 25-27 October 2022 - **oral presentation.**

4. **Melt electrowritten scaffolds for bone surface reconstruction**, Carmen-Valentina Nicolae, Elena Olăreț, Izabela-Cristina Stancu - *BPC, 3rd International Conference on Bioengineering and Polymer Science*, 7-10 june 2023, Bucharest, Romania - **poster presentation**.

5. **Development of bioinspired printable nanostructured formulations for bone tissue regeneration**, Carmen-Valentina Nicolae, Andrada Serafim, Cristina-Elena Stavarache, Raluca-Elena Ginghină, Doris Steinmüller-Nethl, Justus Lackner, Kristin Syverud, Monica Sandri, Kamal Mustafa, Ahmad Rashad, Izabela-Cristina Stancu - *BPC, 3rd International Conference on Bioengineering and Polymer Science*, 7-10 june 2023, Bucharest, Romania - **oral presentation**.

6. **Enhanced Bone Surface Reconstruction Using Thin Melt Electrowritten Reinforced Scaffolds**, Carmen-Valentina Nicolae, Elena Olăreț, Izabela-Cristina Stancu - CheMeet, 26-28 June 2023, online - **oral presentation**.

7. **Nanodiamond-driven potential modulation of cellular response through local (nano)mechanical reinforcement of 3D printed gellan gum scaffolds**, Carmen-Valentina Nicolae, Elena Olăreț, Raluca-Elena Ginghină, Sorina Dinescu, Andrada Serafim, Izabela-Cristina Stancu - *Transnational Multiplier Event*, 18-19 Octombrie 2023, online - **poster presentation**.

8. **The Potential of Nanodiamond Particles to Orchestrate the Cellular Behavior and Modulate the (Nano)Mechanical Properties of 3D Printed Scaffolds**, Carmen-Valentina Nicolae, Elena Olăreț, Raluca-Elena Ginghină, Sorina Dinescu, Andrada Serafim, Izabela-Cristina Stancu - *ESB2023 - 33rd Annual Conference of the European Society for Biomaterials*, 4-8 September 2023, Davos, Switzerland - **poster and Rapid Fire oral presentation**.

9. **Exploring potential nanoparticle effects on cellular response in 3D printed scaffolds through local nanomechanical reinforcement,** Carmen-Valentina Nicolae, Elena Olăreț, Raluca Elena Ginghină, Sorina Dinescu, Andrada Serafim, Izabela Cristina Stancu - *TUIASI 2024 - International Conference of the Doctoral School, „Gheorghe Asachi" Technical University of Iași*, 15-17 mai 2024, online - **oral presentation**.

10. **Nanostructured Multicomponent Bioinks with Synergistic Nanodiamond and Magnesium-Doped Hydroxyapatite for Enhanced Bone Tissue Engineering**, Carmen-Valentina Nicolae,

Masoumeh Jahani Kadousaraei, Mehmet Serhat Aydin, Shuntaro Yamada, Niyaz Al-Sharabi, Ahmad Rashad, Elisabetta Campodoni, Monica Sandri, Doris Steinmüller-Nethl, Kristin Syverud, Kamal Mustafa, Izabela-Cristina Stancu - *NanoBioMat 2024, Applications of Chemistry in Nanosciences and Biomaterials Engineering,* 27-29 November 2024 - **oral presentation**.

11. **Enhancing Cellular Interactions through Bioactivation and Local Nanomechanical Reinforcement in Nanodiamond-loaded 3D Printed Scaffolds**, Carmen-Valentina Nicolae, Elena Olăreț, Raluca-Elena Ginghină, Sorina Dinescu, Andrada Serafim, Masoumeh Jahani Kadousaraei, Mehmet Serhat Aydin, Kamal Mustafa, Izabela-Cristina Stancu - *RICCCE 2024 - 23rd Romanian International Conference on Chemistry and Chemical Engineering*, 4-7 September 2024, Constanța, Romania - **oral presentation**.

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