Registration number,
"Petru Poni" Institute
of Macromolecular Chemistry

3325/30.06.2022

SYNTHETIC SCIENTIFIC REPORT
PN-III-P4-ID-PCCF-2016-0050 Project. Contract no. 4/2018.
-- 2018 ÷ 2022 --

Mimicking Living Matter Mechanisms by Five-dimensional Chemistry Approaches

Mimarea mecanismelor viului prin abordări ale chimiei supramoleculare, în cinci dimensiuni

Acronym: 5D-nanoP

Project WEB site: https://www.intelcentru.ro/5D-nanoP/ro/ and https://www.intelcentru.ro/5D-nanoP/

The project summary page: https://www.intelcentru.ro/5D-nanoP/outline/

The MAIN OBJECTIVE of the project: ***Development of a strategy to synthesize and test (macro)molecular entities of dynamic (re)organizing type, able to act as nanoplatforms of biologic and biomedical relevance.***

The PRAGMATIC APPROACH of the project: ***Defining of a working strategy in the advanced sphere of molecular medicine, to implement, in a biomimetic approach, feasible variants of supramolecular dynamic adaptive systems applicable for targeted intervention in ailing conditions.***

CO - Coordinating Institute - "Petru Poni" Institute of Macromolecular Chemistry, Iasi, Romania

Project Director,
Prof. Aatto Laaksonen

P1 - "Petru Poni" Institute of Macromolecular Chemistry, Iasi, Romania (Responsible partner: prof. Claudiu Supuran)
P2 - "Petru Poni" Institute of Macromolecular Chemistry, Iasi, Romania (Responsible partner: dr. Ioan Cianga)
P3 - "Petru Poni" Institute of Macromolecular Chemistry, Iasi, Romania (Responsible partner: dr. Gheorghe Fundueanu)
P4 - "Petru Poni" Institute of Macromolecular Chemistry, Iasi, Romania (Responsible partner: dr. Maria Cazacu)
P5 - Institute of Cellular Biology and Pathology "Nicolae Simionescu", Bucharest, Romania (Responsible partner: acad. Maya Simionescu)P
P6 – "Costin D. Nenitescu" Institute of Organic Chemistry, Bucharest, Romania (Responsible partner: dr. Calin Deleanu)

Contents

I. The project objectives

The pivotal aim of the **5D-nanoP** project was to contribute to the emerging field of biomimetics, by advanced approaches of supramolecular chemistry, in a strong multi- and inter-disciplinary context. The main objective was to develop a strategy, embodied in a set of protocols, to synthesize and test (macro)molecular entities of dynamic (re)organizing type, able to act as nanoplatforms of biologic and biomedical relevance.

II. The project frame

Mimicking the living matter mechanism of cooperation by complementarity represents one of the most challenging tasks of supramolecular chemistry. The momentary solution consists in using particularly designed molecular unimers, endowed with the necessary amount of chemical information.

The **5D-nanoP** project was dedicated to interfacing the fundamental research area of *constitutional dynamic chemistry* with the practical approaches of *medicinal chemistry* and *biomedical applications*. In the spirit of a metaphor of Jean-Marie Lehn (Nobel Prize in Chemistry, 1987), ***the project aimed to materialize the concept of 5D chemistry in designing, synthesizing, characterizing, and using molecules with conditional affinity, to build versatile supramolecular nanoplatforms able to vectorize compounds of pharmaceutical or biochemical relevance***, involved in physiologic and pathologic processes at cell- and/or tissue-level.

The project succeeded in adding the layer of 5D chemistry over the backgrounds of molecular assembling techniques, to produce macromolecular nanoplatforms, self-assemblable in virtue of the chemical information stored by the designed unimer molecules. In order to prove the applicability of the produced nanoplatforms, an *ex vivo* cell cultivation system was developed, to emulate tissue/tumor niches.

Seven teams were involved in the **5D-nanoP** project, to cover the main addressed research areas: (**i**) the *in silico* molecular design, (**ii**) the development of unimers chemical libraries, (**iii**) the development of macromolecular nanoplatforms, (**iv**) the conjugation of the developed nanoplatforms with chemical species of biomedical interest, (**v**) the build of *ex vivo* emulating niches, and (**vi**) the bio-oriented assessment of the nanoconstructs efficacy. Accordingly, *seven main tasks* were stipulated to be collaboratively followed: (**i**) the *in silico* based design of molecular structures and interactions, and the accurate simulation of molecular edifices and functionality of the synthesized entities, throughout project evolution; (**ii**) the engender of a chemical library of potentially and certified unimers, active according to supramolecular chemistry principles of nanoplatforms building; (**iii**) the selection and the proofing of particular components of the designed nanoplatforms, endowed with the ability of reversibly bonding in physiological or pathological conditions; (**iv**) the effective synthesis of the active nanoplatforms in mimicking assumptions; (**v**) the prospection of dedicated tests associated with the synthesized nanoplatforms, able to evaluate the characteristics and the applications-oriented performances of nanoplatforms as a whole, or of their (released) components; (**vi**) the performing of medicinal chemistry and biological oriented tests that involve the developed nanoplatforms, to assess their functionality and to prove their biocompatibility; (**vii**) the

applicative assembling of the designed nanoplatforms to test them according to their foreseen functionality, including in/inside simulated environments (like the surrogates of tissues or tumors are). ***Figure 1*** depicts the philosophy that inspired the 5D-nanoP project.

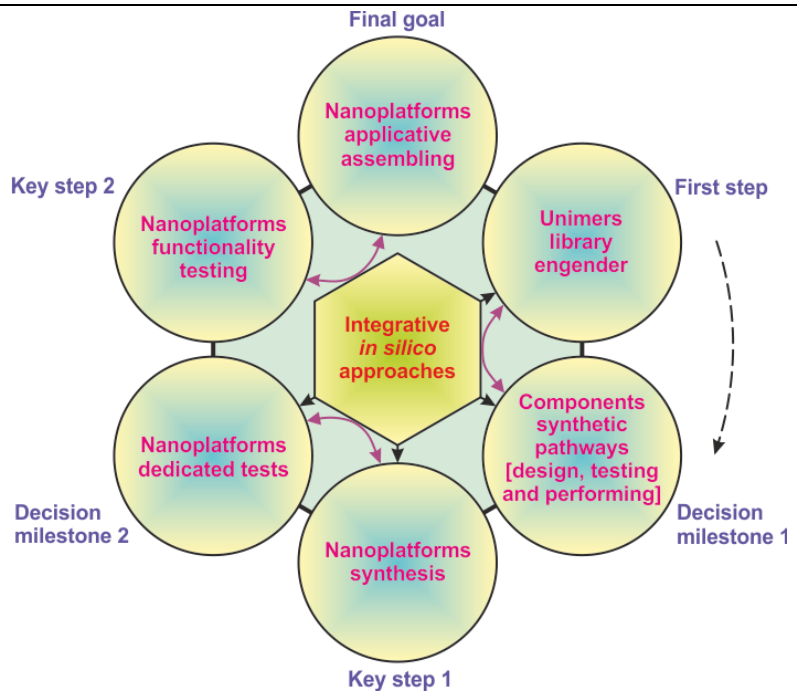


Figure 1. *The philosophy of 5D-nanoP project expressed as networked tasks.*

The project defined *nanoplatforms* as being *compositionally, structurally, and functionally reproducible tri-dimensional (macro)molecular edifices, specifically designed and synthetically generated to perform particular functions*. 5D-nanoP project considered the particular case of *nanoplatforms of assembling-line type*, distinctively dedicated to producing nanomedicines, in a biomimetic approach to emulate some functions of intracellular entities which facilitate the reproducible supramolecular assembling of biochemical actuators.

Starting from the above description of the structure and roles of nanoplatforms, the specific framework of 5D-nanoP project has made use of the following approaches:

(a). definition of the strategy of nanoplatforms composing and building;
(b). selection, synthesis, and characterization of the dynamically linkable unimers, followed by the construction of a library of potential unimers;
(c). selection, synthesis, and versatility proofing of macromolecular substrata able to act as components of functional nanoplatforms;
(d). extensive chemical modelling of all the nanoplatforms components, together with their interactions and functionality, both mutual and with biologic ligands;
(e). perfecting of detailed laboratory protocols regarding the synthesis and modification of the designed nanoplatforms;
(f). development of dedicated protocols for the proofing of nanoplatforms composition, functionality, and interaction with biological milieu (including the cytotoxicity and the complexation with cell/tissue/tumor specific ligands);
(g). development of particular assays to evaluate the reproducibility of nanoplatforms characteristics (during- and after-synthesis), structure, and functionality, together with the design of laboratory protocols to quantitate the nanoplatforms amount and activity;
(h). development of particular surrogates of biological milieus for testing the nanoplatforms.

III. Scientific results and achievements of 5D-nanoP project

In order to report them, the results of 5D-nanoP project will be divided in the four main achievements which have emerged as original scientific contributions. Only the most relevant results will be included below, in a recapitulative style, based on the previous stages reports.

III.1. Unimers synthesis, selection, characterization, and use

We selected the ***carbonic anhydrases inhibitors*** (CAIs) as a prototypical unimers class for both (**i**) the assembling of functional nanoplatforms, and (**ii**) the building of assembled nanoentities of biomedical relevance. CAIs belong to a large variety of chemotypes possessing a wealth of inhibition mechanisms and are already clinically used for the management of different disorders. Therefore, they are relevant as components of potential nanomedicines. This is why we choose to develop and test them as components of supramolecular active aggregates.

Selenazoles represent one of the CAIs classes we synthesized, characterized and tested as potential antimicrobials able to fight against multidrug-resistance towards classical antibiotic. ***Figure 2*** depicts the synthetic pathways of the investigated selenazoles [1].

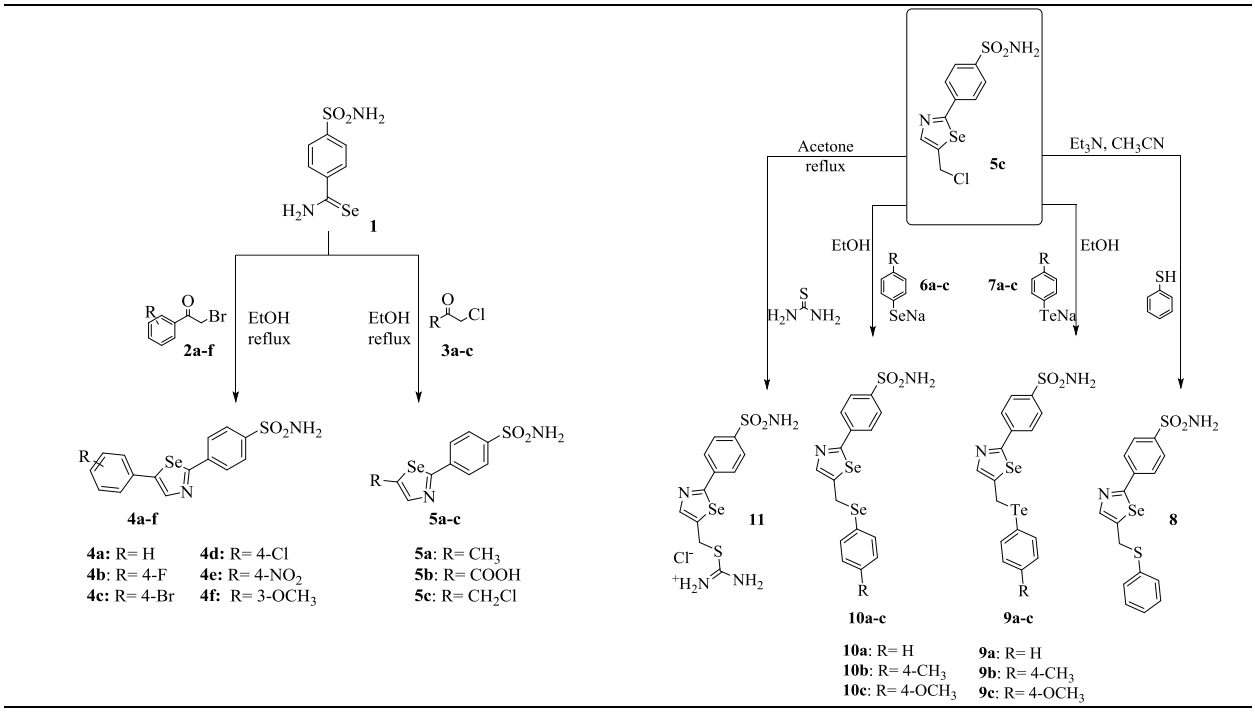


Figure 2. *Unsubstituted and substituted selenazoles used as inhibitors in the studies on the structure-activity relationship related to the inhibition of different CAs classes from different pathogenic bacteria.*

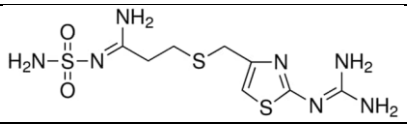


Figure 3. *Famotidine tested as versatile anti-microorganism CAI.*

We investigated the inhibitory effects of famotidine (***Figure 3***) against all classes of CAs from the pathogenic bacteria *Vibrio cholerae*, *Burkholderia pseudomallei*, *Mycobacteri-um tuberculosis*, as well as the CAs from the non-pathogenic bacteria/cyanobacteria *Sulfurihydrogenibium yellowstonensis*, *S. azorense*, *Pseudoalteromonas haloplanktis*, *Colwellia psychrerythraea*, *Nostoc commune*, diatom *Thalassiosira weissflogii*, fungi *Cryptococcus neoformans*, *Candida glabrata* and *Malassezia globosa*, *Trypanosoma cruzi* and *Plasmodium falciparum* protozoans, and *Anopheles gambiae* mosquito [2].

We also developed ***unimers capable of intrinsically acting as CAIs*** [3]. ***Figure 4*** sketches the involved reactions. CAIs-squalene derivatives can act as self-assembling unimers.

A library of ***CAIs of chalcogene-bearing type*** was developed and tested as antimicrobials and as antitumorals. ***Figures 5, 6 and 7*** include examples of the library members [4, 5].

III.2. Synthesis and testing of nanoplatforms components. Nanoplatforms assembling.

We started by the design, synthesis and characterization of heterografted, amphiphilic, "Hairy-Rod"-like polythiophenes capable to act as ***electroactive surfaces and nanoplatforms for biomedical applications***. ***Figure 8*** summarizes the synthesis steps of a PTh-*graft*-(PEG-*rand*-PCL) copolymer having a hairy morphology which is *a priori* appropriate to function as nanoplatforms of assembling-line type [6].

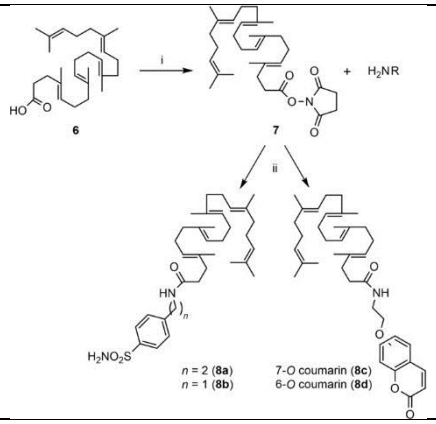


Figure 4. *Two steps synthesis pathway of CAI-squalene derivatives.*
(i) *EDC·Cl, NHS, DMF dry, RT, 2÷4 h;*
(ii) *Et3N, dry DMF, RT, 12÷24 h.*

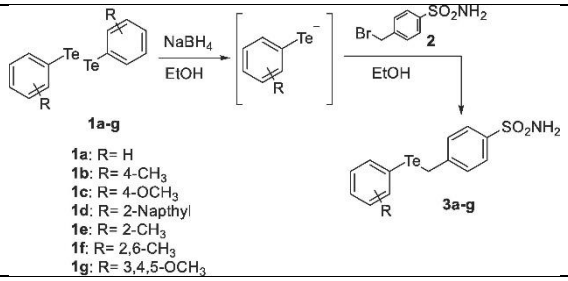


Figure 5. *Members of a CAIs library of tellurides type.*

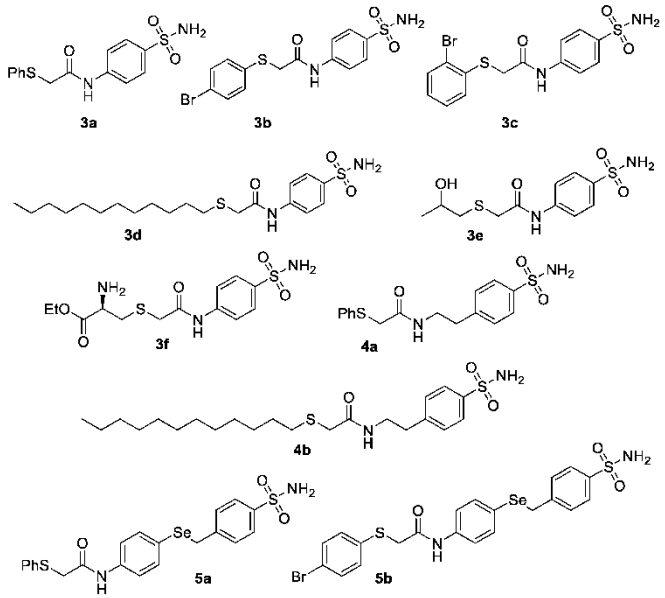


Figure 6. *Members of a CAIs library of sulphur-containing type.*

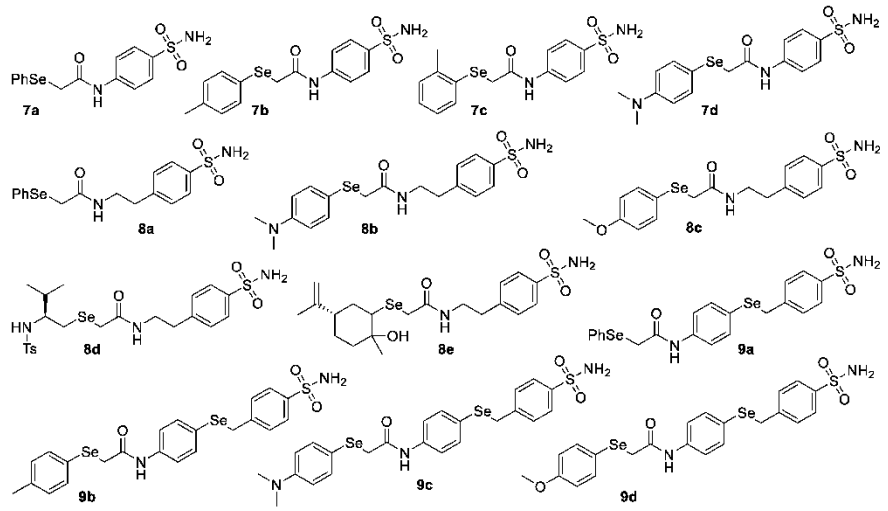


Figure 7. *Members of a CAIs library of selenium-containing type.*

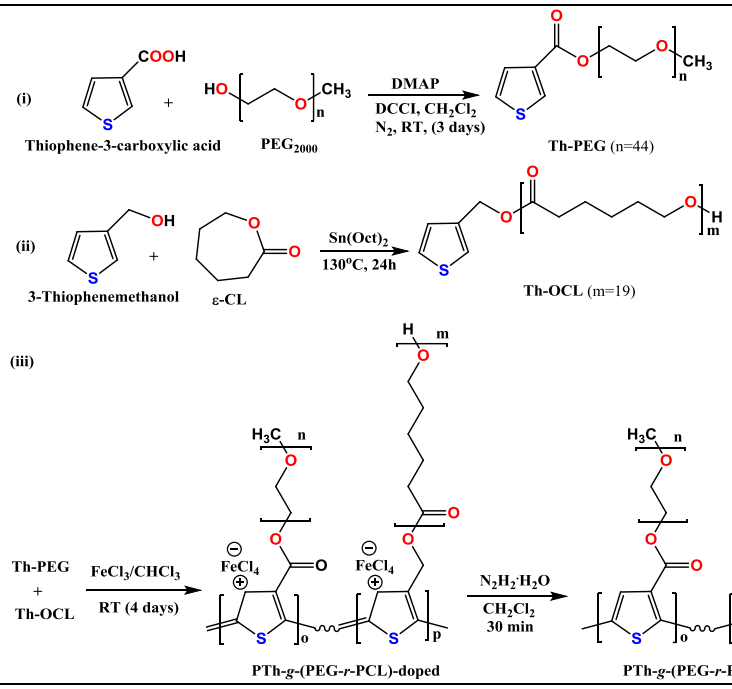


Figure 8. *Synthesis of PTh-g-(PEG-r-PCL) copolymer.*

(i) *Esterification reaction of thiophene derivative and PEG2000.*

(ii) *Ring-opening polymerization of ε-caprolactone initiated by thiophene-methanol.*

(iii) *oxidative polymerization of macromonomers from* ***(i)*** *and* ***(ii)*** *and reaction with hydrazine.*

We have further studied the ways of producing ***chain extenders capped with versatile moieties***, that can be attached to the PTh-g-(PEG-r-PCL) nanoplatforms, or that can directly function as nanoplatforms of irregular type [7]. ***Figure 9*** includes the synthesis pathway of a phenothiazine derivative.

Solid nanoparticulate platforms of silica-functionalized type were also studied [8]. ***Figure 10*** depicts the synthesis pathway of such a product. The chemical modification of SH groups with allyloxyethylene-glucopyranoside has been performed by thiol-ene addition, combined with ultrasound treatment, in water, in the presence of 2,2-dimethoxy-2-phenylacetophenone as a photo initiator. The modified silica was separated and repeatedly washed with water to remove the un-reacted glucose derivative.

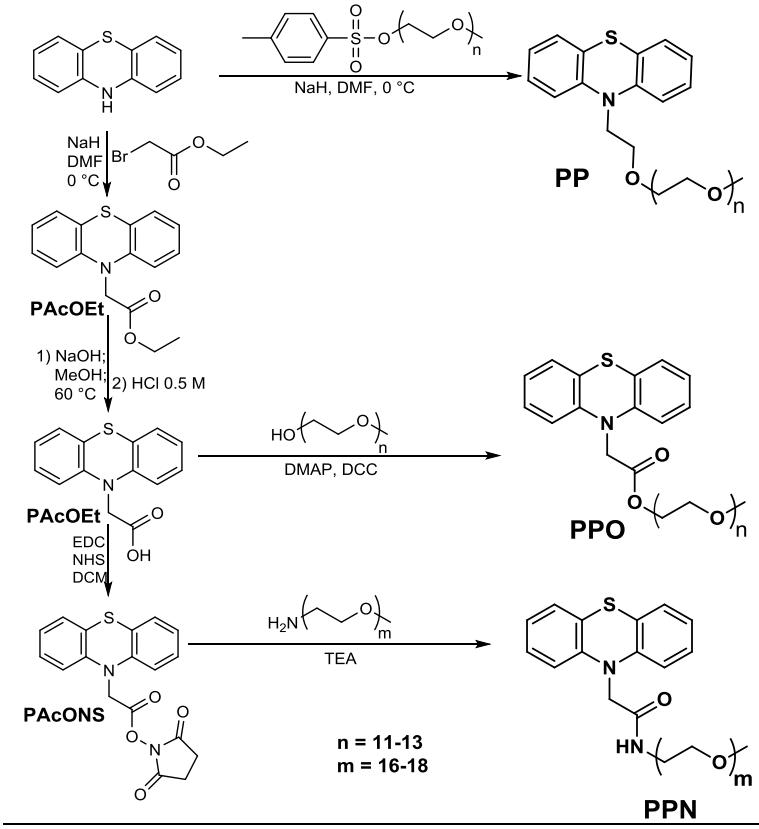


Figure 9. *The synthesis scheme of PEG-phenothiazine derivatives.*

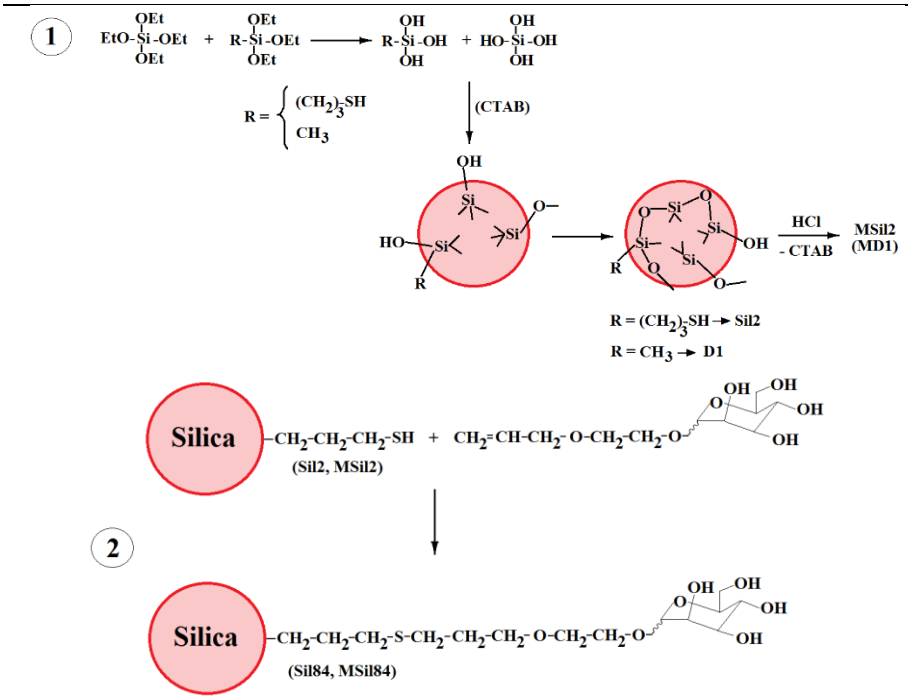


Figure 10. *The synthesis of thiol- and glucose-functionalized silica derivatized nanoplatforms [8].*

Bioactive platforms based on electroresponsive nanoentities were developed with the aim of constructing versatile substrata for the extemporaneous preparation of injectable nanoentities according to the philosophy of (macro)molecular assembling-line. ***Figure 11*** describes the principles of preparation of a bioplatform of *iso*-PPf/PEDOT-*graft*-PCL type [9], that includes an isotactic polypropylene film (iPPf) coated with poly(3,4-ethylenedioxythiophene) grafted with poly(ε-caprolactone) chains (PEDOT-*graft*-PCL). PEDOT-PCL moiety acts as a biocompatible interface, which can host various bioactive molecules, including CAIs. The bioactive platforms were characterized by physical-chemical (FTIR, Raman, surface energy, thermal analysis, dynamic mechanical analysis), electrochemical (voltammetry, amperometry), imaging (SEM and AFM,), and biologic (cytocompatibility, cellular adhesion (see ***Figure 12***), cell proliferation) techniques.

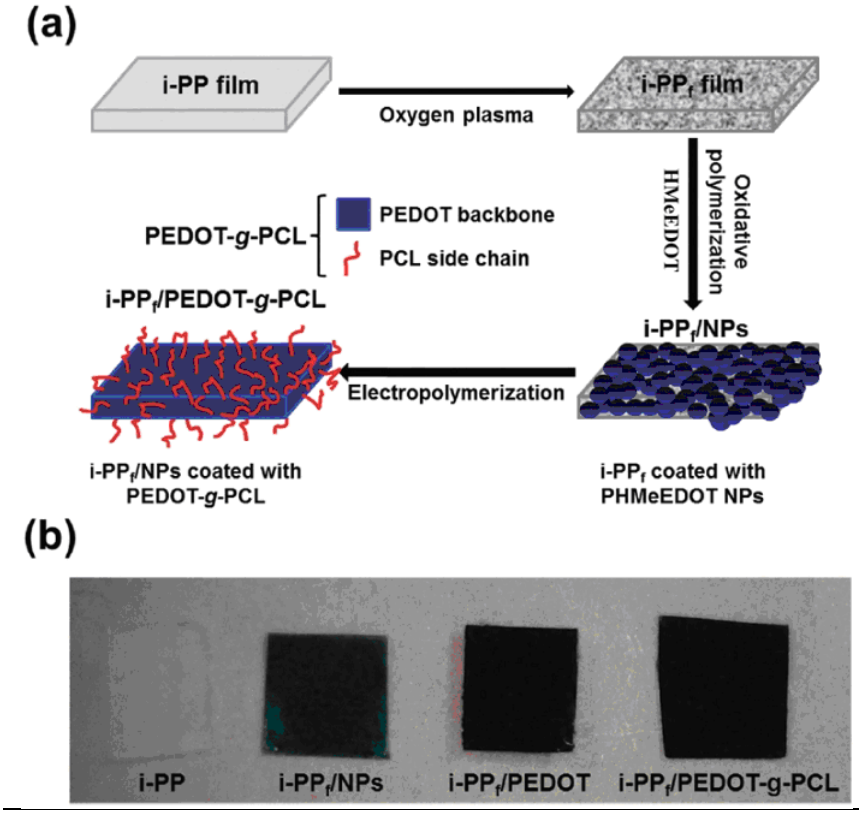


Figure 11.
(a) *The three steps used to prepare the i-PPf/PEDOT-g-PCL bioplatforms.*

(b) *Photographs of pristine i-PP, i-PPf/NP, i-PPf/ PEDOT and i-PPf/PEDOT-g-PCL films.*

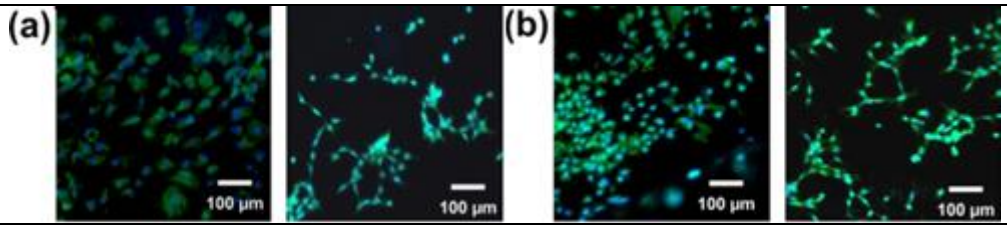


Figure 12. *Cells adhesion and proliferation on the bioactive platforms surface.*
(a) *i-PPf/PEDOT.* ***(b)*** *i-PPf/PCL-g-PCL.*
SEM micrographs and 2D AFM height and phase contrast images.

III.3. Development and characterization of systems for *ex vivo* nanoplatforms testing

Four types of surrogates of connective tissues and tumors were investigated: (**i**) hydrogels of ternary mixtures of collagen / hyaluronic acid / poly(ε-caprolactone) post-processed to be transformed in various substrata (***Figure 13*** [10]), (**ii**) hydrogels of poloxamer-*graft*-carboxymethyl pullulan (***Figures 14*** *and* ***15*** [11]), (**iii**) hydrogels based on hyaluronic acid (HA) and poly(methylvinylether-alt-maleic acid) (P(MVEaltMA)) [12, 13**]**), and silatrane-based [8]. All of them were prepared as ***3D bioavailable constructs***.

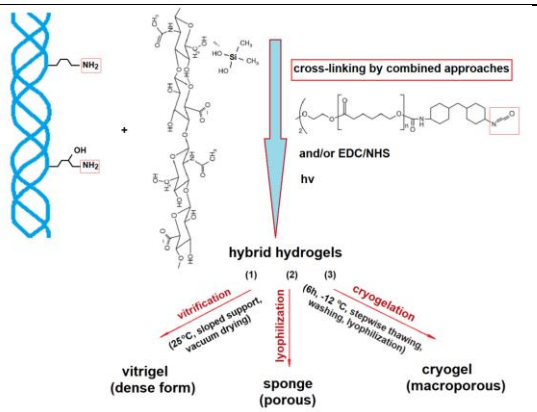


Figure 13*. Schematic representation of the preparative protocol for the investigated hybrid 3D constructs.*

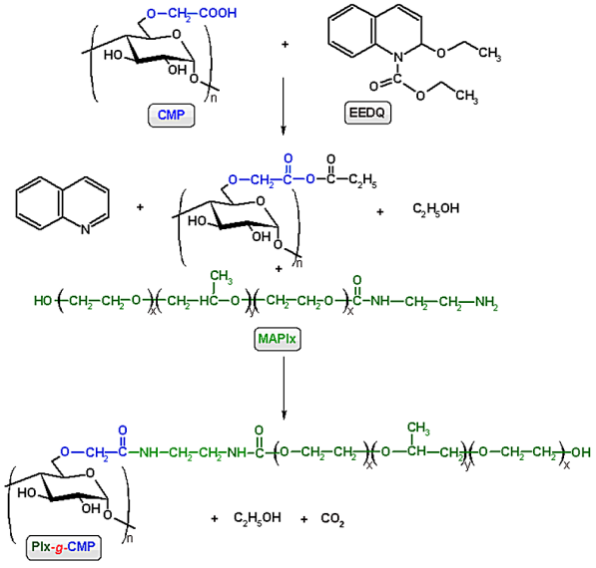


Figure 14*. Synthesis route of poloxamer-graft-carboxymethyl pullulan copolymer.*

Poloxamer 407 (Pluronic F-127) was used (among other ones tested).

The functional performances of the surrogates of poloxamer-graft-carboxymethyl pullulan copolymer type (Plx-*g*-CMP) were evaluated compared to an alginate/poloxamer hydrogel previously developed by us and successfully tested as a keratinocyte proliferation promoter. ***Figure 16*** presents the results of human skin fibroblasts accommodation on the surface of the Poloxamer 407 containing copolymer. The synthesized copolymer is cytocompatible at concentrations of 0.3125 ÷1.25 mg/mL during 48 hours of incubation and becomes highly cytotoxic at concentrations above 2.5 mg/mL. In the range of

cytocompatibility, the poloxamer-*graft*-carboxymethyl pullulan hydrogel does not modify the cellular morphology of fibroblasts, being applicable both for ex vivo cell cultivation and for tissue engineering application as a scaffold for connective tissue replacement.

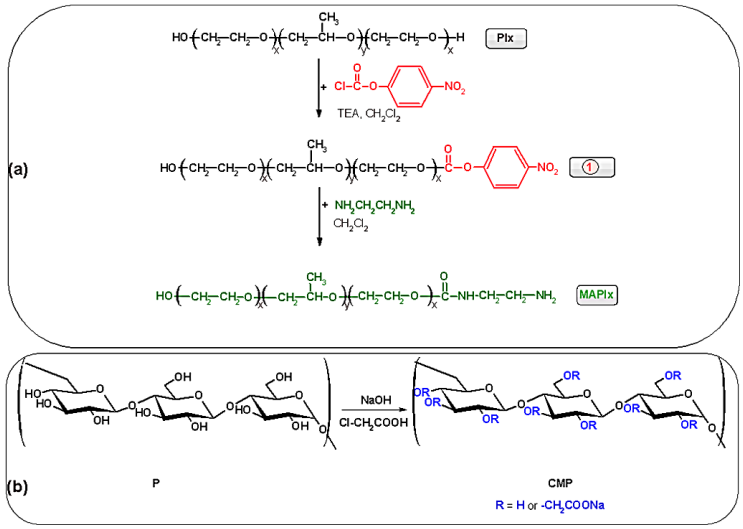


***Figure 15**. Synthesis route of monoamine derivative of poloxamer (MAPlx) (a) and carboxymethyl pullulan (b).*

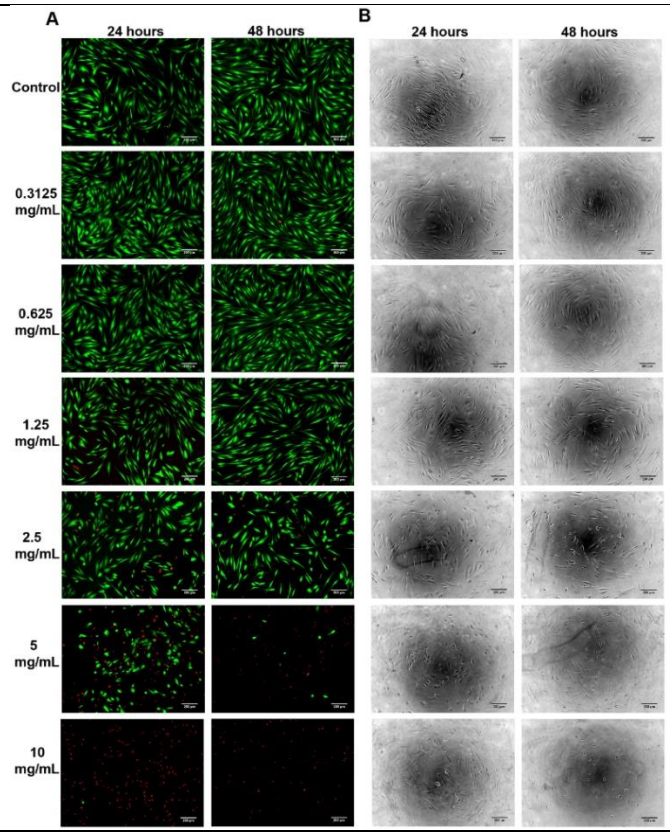


***Figure 16.** Merged live (green) / dead (red) cell images (**A**) and cell morphology (**B**) of fibroblasts exposed to various concentrations of poloxamer-graft-carboxymethyl pullulan copolymer. Scale bar: 200 µm.*

Hydrogels based on hyaluronic acid (HA) and poly(methylvinylether-alt-maleic acid) were proved to be suitable for chemotherapeutic drug testing on hepatocellular carcinoma (***Figure 17***) [12, 13]. Compared to 2D, the cells grown in the hyaluronic acid-based scaffold proliferate into larger-cellular aggregates that exhibit liver-like functions. Also, growing the cells in the scaffold sensitize the hepatocytes to the anti-tumor effect of cisplatin, by a mechanism involving the activation of ERK/p38α-MAPK and dysregulation of NF-kB/STAT3/Bcl-2 pathways. Moreover, the system can be adapted and employed as experimental platform functioning as a proper tissue/tumor surrogate.

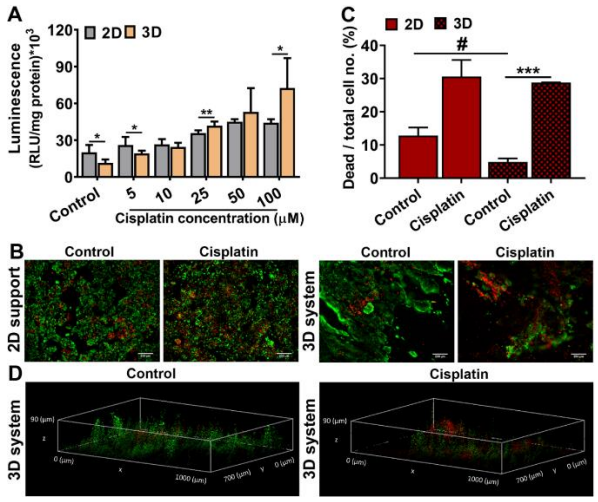
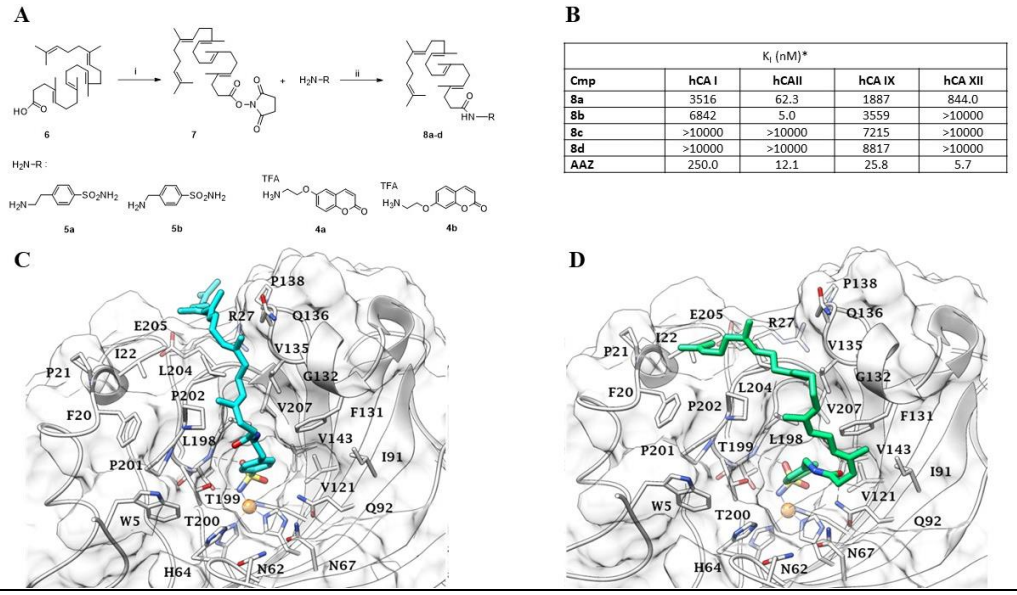


Figure 17*. Cisplatin-induced cytotoxicity in HepG2 cells cultured on 2D support and in the hyaluronic acid-based scaffold (3D). HepG2 cells grown on 2D and in 3D systems for 7 days were exposed for 24 hours to 5-100 μM cisplatin or 0.1% DMSO (control cells). (A) The cisplatin cytotoxicity in HepG2 cells was investigated by the release of the adenylate kinase in the culture medium. (B) Live (green)/dead (red) assay of control cells and 25 μM cisplatin-treated HepG2 cells. Scale bar: 200 μm. (C) The percentage of dead/total cell number obtained by live/dead cell assay. (D) 3D reconstruction images of the Z-stacking sections for live/dead assay of control and cisplatin-treated HepG2 cells grown in hyaluronic acid scaffold.*

III.4. Computational chemistry techniques for functional (macro)molecules investigation

Improvement of the squalene-based unimers were investigated in order to produce inhibitors of carbonic anhydrases. Squalene derivatives were obtained by coupling reactions of squalene bearing carboxylic group with coumarin and benzenesulfonamide derivatives (***Figure 18.A***) [3]. In vitro evaluation to determine the inhibition profile of human carbonic anhydrases (hCA) isoforms I, II, IX and XII was performed by the stopped flow technique, in the presence of synthesized derivatives. ***Figure 18.B*** resumes the results.

Hybrids containing the benzenesulfonamide function showed high selectivity and an excellent inhibition profile against the hCA II isoform, compared to the other tumor isoforms hCA IX and hCA XII. They also showed much better K_i values than the starting compounds. The excellent inhibitory action of these compounds against hCA II isoform recommends them as potential candidates in preclinical studies for glaucoma or related applications in which hCA II is involved. The performed *in silico* molecular modelling studies regarding the docking of squalene derivatives into the CA II isoform are illustrated in ***Figure 18***.



K_i (nM)*				
Cmp	**hCA I**	**hCAII**	**hCA IX**	**hCA XII**
8a	3516	62.3	1887	844.0
8b	6842	5.0	3559	>10000
8c	>10000	>10000	7215	>10000
8d	>10000	>10000	8817	>10000
AAZ	250.0	12.1	25.8	5.7

Figure 18. *(**A**) The synthesis of squalene derivatives. (**B**) The inhibitory activity of the squalene derivatives against some of the human carbonic anhydrases isoforms. The docking of squalene-sulfonamide derivatives **8a** (**C**) and **8b** (**D**) to the active center of CA II, demonstrated by in silico molecular modelling.*

To correlate chemical structures with the inhibition profile of compounds 8a and 8b, docking and optimization studies were performed with the active centers of CA II (***PDB 5LJT***). The aliphatic chains of compounds 8a and 8b are dispersed in the enzyme mass where they form Van der Waals-type stabilizing

interactions with the residues in the lipophilic half of the active centers I22, F131, V135, P202 and L204 of CA II. Furthermore, the length of the single methylene unit connector between the squalene-linked amide group and the sulfonamide-linked phenyl group (8b) leads to the formation of spaced hydrogen bonds between the –C=O amide of compound 8a and the $–NH_2$ groups in the Q92 side chain of CA II. It is possible that the shorter length of the connector together with the extended network of hydrophobic contacts explains a better inhibition profile of the derivative 13b compared to 13a, where the connector consists of two methylene units [3].

A novel compound was synthesized by linking two pyrene moieties to diaminodibenzo-18-crown-6-ether through –HC=N– bonds, resulting in DPyDB–CH=N–18C6 product [14]. The synthesis of the novel compound was confirmed by FTIR, ^{1}H-NMR, ^{13}C-NMR, TGA, and DSC techniques. The quantitative ^{13}C-NMR analysis revealed the presence of the two position isomers. WAXD technique and MD simulations were used to evaluate the possibility of the supramolecular arrangement of DPyDB–CH=N–18C6. Both experimental and theoretical methods showed that the compound forms an aggregate with weak π–π interactions. The MD computational results indicated the existence of some structures as a slipped-parallel aggregate with non-covalent interaction distance between 3.28 and 3.45. QM results showed that these two isomers were almost is energetically by energetic point of view. Through the QM calculations, it was observed that –C–HC=N–C– dihedral angle, which links the pyrene units to the phenyl rings of the crown ether, was twisted around 40°. This situation explains the inability to align both pyrenes ring from the same DPyDB–C=N–18C6 molecule with the pyrenes from another molecule, as observed from the MD simulation results. This incapacity is also governed by the presence of a C–H bonds and lone pairs of nitrogen from the –HC=N– bond, inducing a hindrance repulsion between individual molecules. Moreover, the DPyDB–C=N–18C6 compound was investigated from the point of view of its photophysical properties. In order to understand the electronic structure, the UV-vis and fluorescence experiments together with the theoretical studies (QM calculations) were performed in solvents with different polarities (n-hexane, toluene, 1,2-dichloroethane, and ethanol). From these data, we observed the presence of $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, among which the $\pi \rightarrow \pi^*$ transition due to π-extended conjugation is predominant. By contrast, through fluorescence analysis, a weak emission was observed and could be explained by photoinduced electron transfer (PET) and aggregation caused by quenching (ACQ) effects. The frontier molecular orbitals into the ground state demonstrated that the electronic density of DPyDB–C=N–18C6 was localized only on one pyrene–CH=N–phenyl sequence of the crown ether, leading to a perturbation of a well-ordered intermolecular π–π stacking.

Another direction was to investigate the conformational effect of target compounds. Computational results (based on DFT-PBE0/6311+G(d,p)) indicate that the conformation trans-cis isomer was the most stable by energetically point of view (***Figure 19***). The electronic representations in ground state as well as into excited state were localized on pyrene and benzene units. As an effect of excitation, the electron density was delocalized from –CH=N-benzene to pyrene sequence due to the charge transfer. In all three conformations trans-trans, trans-cis and cis-cis the charge transfer effect was observed. Also, the theoretical results used CAM-B3LYP indicated the presence of $\pi \rightarrow \pi$ and $\pi \rightarrow \pi^*$ transitions due to π-extended conjugation. All theoretical results are in agreement with the experimental determinations.

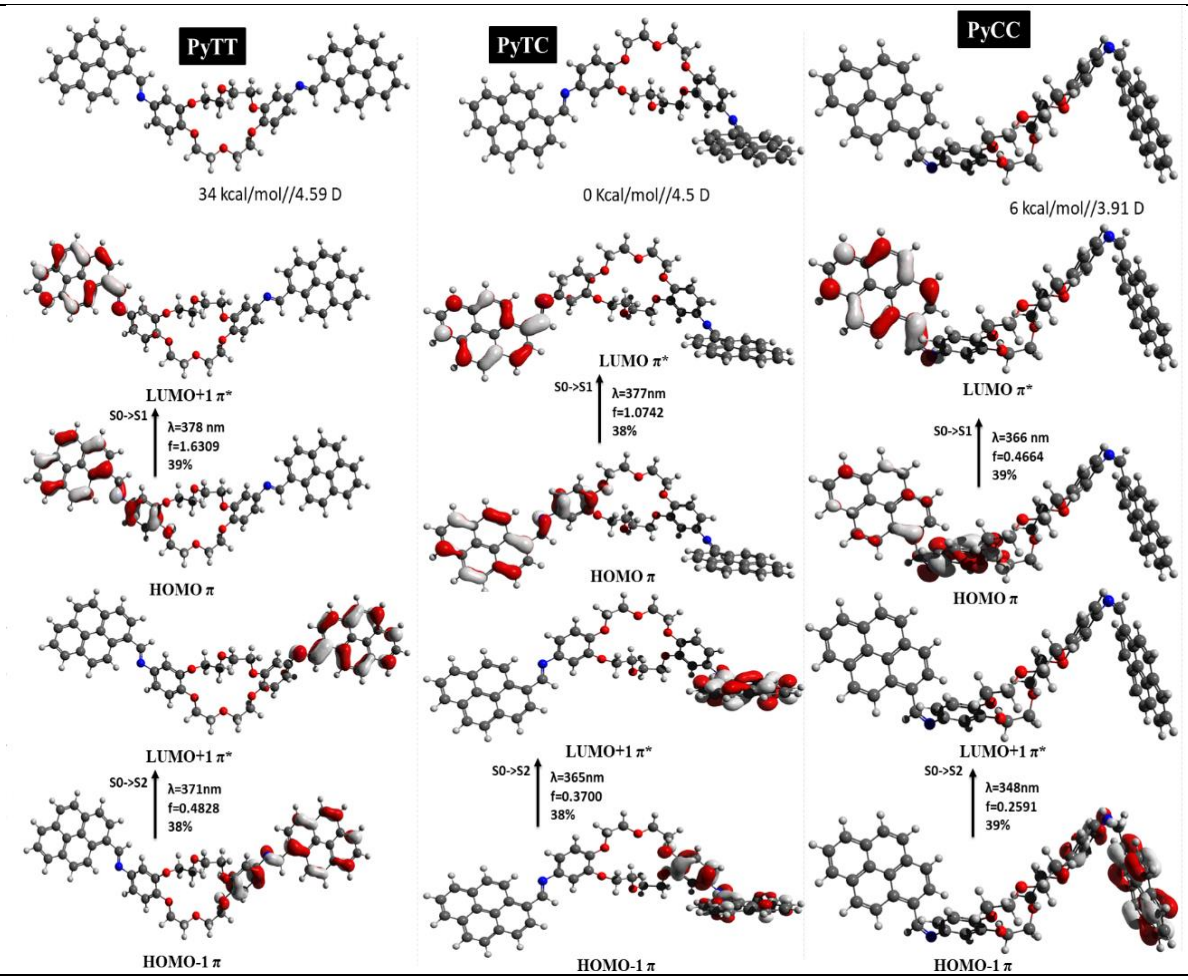


Figure 19. *Electronic structure of DPyDB–C=N–18C6 taking into consideration trans-trans, trans-cis, and cis-cis conformations.*

IV. Dissemination in terms of remarkable publications

The dissemination of the 5D-nanoP project is loaded as annexes of this report and on the project WEB site (**https://www.intelcentru.ro/5D-nanoP/)**.

V. Estimated impact of the 5D-nanoP project, and the most prominent result

The positive impact of the project is expected to cover scientific, industrial, health care and societal fields. From a scientific point of view, the project results are expected to accredit the use of supramolecular dynamic aggregates as key functional components of bioplatforms of different types, including of assembling-line type, in producing therapeutic nanoconstructs according to the principles of nanomedicine.

One of the immediate impacts resulted by using these materials for *in vitro* characterization of living systems. The already obtained feedback is expected to contribute to the improvement, on the design of the polymer biomedical materials.

The foreseen economic impact derives from the long-awaited knowledge transfer toward clinical and public health applications, and even towards the pharmaceutical industry and market. In this respect, the chemically engineered new carbonic anhydrases inhibitors, silica and conductive polymers (also useful for biointerfacing and bioelectronics) and nanoconjugates are expected to function as high-performance platforms for the effective encapsulation and sustained release of drugs and genes. Moreover, the proposed alternatives for the synthesis of new nanoconjugates could have a less negative impact on the environment.

By approaching compounds containing silicon, the carbon isoster, contributions have been made to expanding the chemical space available for medical chemistry, by creating new options for the

development of new delivering, targeting and directly-active systems. The hypervalent silicon functionality should also allow for new approaches to the molecular design of biologically-active nanoconstructs.

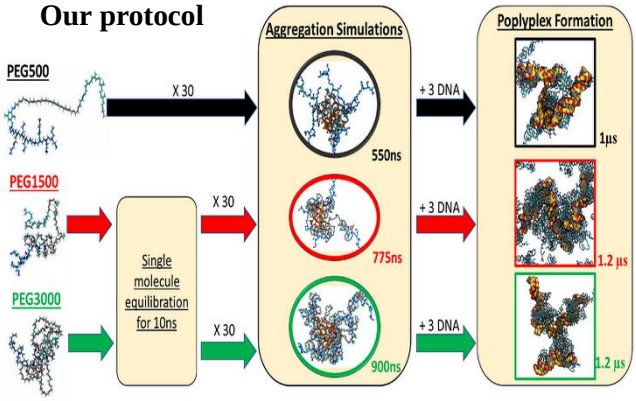
The systems for *ex vivo* testing of nano-medicines are constantly expanding. 5D-nanoP project has developed, tested, and characterized several types of tissue and tumor surrogates with potential applications both in drug development and in tissue engineering.

Advanced achievements results obtained during the progress development of 5D-nanoP project, published in ISI indexed journals (more than 100 ISI papers were published, with an average of more than 6 IF, and some of them with very high IF, for example, *Renewable & Sustainable Energy Reviews* (IF: 16.799) and *Chemical Reviews* (IF: 72.087)), were noticed (cited) by the international scientific community working on the emerging fields. As a result, 5D-nanoP project already had an immediate academic impact.

V.A. Representative results in terms of *in silico* simulation

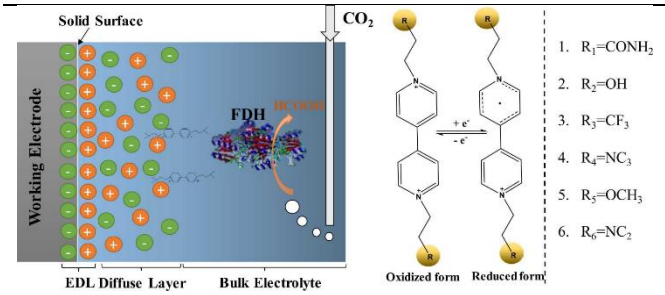
1. Vasiliu T., Craciun B.F., Neamtu A., Clima L., Isac D.L., Maier S.S., Pinteala M., Mocci F., Laaksonen A., *In silico* study of PEI-PEG-squalene-dsDNA polyplex formation: the delicate role of the PEG length in the binding of PEI to DNA, *Biomaterials Science* 9, **2021**, 6623-6640. DOI: 10.1039/d1bm00973g (**IF: 7.59**)

Schematic representation of the simulation protocol of the polyplex formation, for the three studied vectors represented on the left from top to bottom: PEG500, PEG1500, PEG3000. The first step of the simulations for PEG aimed at reproducing the aggregation of 30 vector molecules, while for PEG1500 and PEG3000 a single vector molecule was equilibrated in water for 10 ns before putting together 30 vector molecules. Stable aggregates were obtained after 550–900 ns of MD simulation, depending on the size of the vector. 3 DNA molecules were added to the equilibrated vector, and MD simulations of in the μs timescale were performed.



Our simulations demonstrate that equilibrating the vector solution, with several hundreds of ns long MD, prior to adding the DNA leads to the formation of a large network of interactions between the vector components, which are largely kept also after the addition of DNA and thus have an important role in its binding. The employed two-step simulation approach mimics the experimental procedure and gives a better understanding of all the mechanisms having a role in DNA binding. All the simulations were found in agreement with the experimental measurements, with the final aggregates of the vectors obtained in the simulation explaining the zeta potential results, and the trends observed in DNA binding matched the trends obtained in the gel electrophoresis experiment. These findings have important implications for the rational design of non-viral genetic vectors, revealing, at the molecular level, how the molecular mass of the widely used stealth agent, PEG, affects the nucleic acid binding to the cationic polymers.

2. Zhang Z., Vasiliu T., Li F., Laaksonen A., Zhang X., Mocci F., Ji X., Novel artificial ionic cofactors for efficient electro-enzymatic conversion of CO2 to formic acid, *Journal of CO2 Utilization* 60, **2022**, 101978 (**IF: 8.321**)

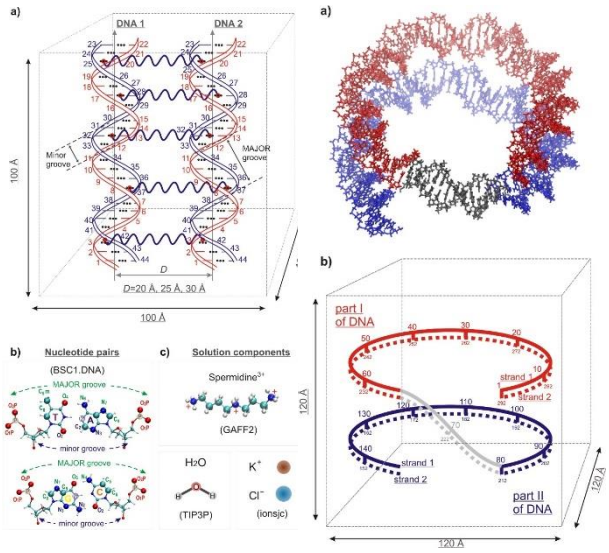


Electroenzymatic conversion of CO_2 to formic acid, and chemical structures of the studied bipyridinium-based redox cofactors.

In this study, six artificial cofactors were designed and synthesized for the enzymatic CO_2 reduction to formic acid. All the bipyridinium-based artificial cofactors presented a superior catalytic performance

compared to the natural cofactor NADH, owing to the suppression of the reverse oxidation reaction. Specifically, the formic acid concentration by using the cofactor $BPNC_2$ is 47 times higher than that of NADH. MD simulations give further molecular insight into the behavior of the cofactor, confirming $BPNC_2$ with the highest affinity of CO_2, which is consistent with the experimental observations. Last, ab initio calculations indicate that the functional groups R also affect the electronic distribution and the electron-donating capability of BP core, and interestingly the positively charged functional groups as NC_2 and NC_3 can surprisingly lead to an increased electron-donating capability of the heavy atoms belonging to the aromatic core, as revealed by the condensed Fukui f^- functions. The different catalytic activity of the artificial cofactors is therefore due to a combination of several contributions, comprising the affinity for CO_2, the effect on the electron-donating capability in the BP rings and also the reactivity of the functional group itself. Our analysis should pave the way for future systematic studies aimed at disentangling the relative weight of each contribution to find a quantitative structure-activity relationship.

3. Vasiliu T., Mocci F., Laaksonen A., De Villiers Engelbrecht L., Perepelytsya S., Caging polycations: Effect of increasing confinement on the modes of interaction of spermidine^{3+} with DNA double helices, *Frontiers in Chemistry* 10, **2022**, 836994. DOI: 10.3389/fchem.2022.836994 (**IF: 5.545**)



(Left) *(**a**) Schematic representation of the simulation box for systems DD-20Å, DD-25Å, DD-30Å, together with the numbering of the nucleotide bases, and the indication of the positioning of the restraints used in the simulation to maintain the initial relative orientation and distance between the DNA helices. (**b**) T-A and C-G base pairs with the label of the atoms used as reference in the analysis. (**c**). Schematic representation of the structure of the solvent and counter- and co-ions of DNA. The force fields used to describe the components are also indicated.* ***(Right)*** *Simulated system of nucleosomal DNA. (**a**) Nucleosomal DNA: red and blue colors indicate the overlapping parts of the DNA double helix, non-overlapping DNA colored grey. (**b**) Schematic structure of the nucleosomal DNA in the simulation box. The numbering of the nucleotide pairs is indicated.*

Four model systems, each containing two DNA double helices with different DNA-DNA distances, in the presence of Spd^{3+} and KCl, have been studied using MD computer simulations, with the aim to understand how the separation between DNA double helices influences the interaction with PAs. Also, the dynamics of the Spd^{3+} molecules are strongly affected by the DNA-DNA separation: at a very short distance (20 Å) the Spd^{3+} located between the DNA molecules are effectively stuck in their binding sites; increasing the inter-helical separation to 25 Å, the PAs still maintain relatively long residence times in the region between the helices, but they move from one binding site to another. Further increasing the separation between the DNA helices to 30 Å leads to a further increase in Spd^{3+} mobility, thus reducing the residence time in the inter-helical space.

V.B. Representative results in terms of synthesis, physical-chemical characterization and biological properties evaluation of the constituents of dynamic assembling supramolecular nanoplatforms

(1) Angeli A., Pinteala M., Maier S.S., Simionescu B.C., Milaneschi A., Abbas G., del Prete S., Capasso C., Capperucci A., Tanini D., Carta F., Supuran, C.T., Evaluation of thio- and seleno-acetamides bearing benzenesulfonamide as inhibitor of carbonic anhydrases from different pathogenic bacteria, *International Journal of Molecular Science* 21 (2), **2020**, 598. DOI: 10.3390/ijms21020598 (**IF: 6.208**); **(2)** Angeli A., Pinteala M., Maier S.S., del Prete S., Capasso C., Simionescu B.C., Supuran C.T., Inhibition of α-, β-, γ-, δ-, ε- and η- class carbonic anhydrases from bacteria, fungi, algae, diatoms and protozoans with famotidine, *Journal of Enzyme Inhibition and Medicinal Chemistry* 34, **2019**, 644-650. DOI: doi:10.1080/14756366.2019.1571273 (**IF: 5.756**); **(3)** Angeli A., Pinteala M., Maier S. S., Toti A., Di Cesare Mannelli L., Ghelardini C., Seleri S, Carta F. Supuran, C.T., Tellurides bearing

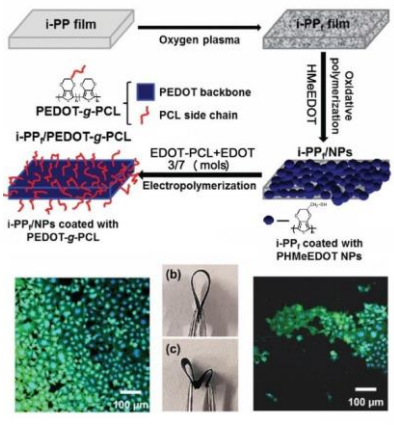
benzensulfonamide as carbonic anhydrase inhibitors with potent antitumor activity, *Bioorganic & Medicinal Chemistry Letters* 45, **2021**, 128147. DOI: 10.1016/j.bmcl.2021.128147 (**IF: 2.94**); **(4)** Clima L., Craciun B.F., Angeli A., Petreni A., Bonardi A., Nocentini A., Carta F., Gratteri P., Pinteala M., Supuran C.T., Synthesis, computational studies and assessment of in vitro activity of squalene derivatives as Carbonic Anhydrase inhibitors, *ChemMedChem* 15, **2020**, 2052-2057. DOI: 10.1002/cmdc.202000500 (**IF: 3.54**)

Members of a CAIs (inhibitors of carbonic anhydrases) library of selenazole, famotidine, tellurides, sulfur and selenium-containing type were synthetized and tested as potential antimicrobials able to fight against multidrug resistance towards classical antibiotics. Some of them were translated at the nanometer scale. In this idea, CAIs-squalene derivatives can act as self-assembling unimmer, demonstrating to be 3–4 times more effective at blocking carbonic anhydrase than necked CAIs.

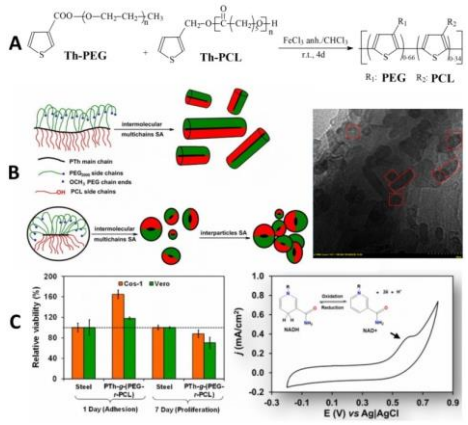
(6) Molina B.G., Cianga L., Bendrea A.-D., Cianga I., Aleman C., Armelin E., An amphiphilic, heterografted polythiophene copolymer containing biocompatible /biodegradable side chains for use as (electro) active surface in biomedical applications, *Polymer Chemistry* 10, **2019**, 5010-5022; DOI:10.1039/C9PY00926D (**IF: 5.364**); **(7)** Molina B.G., Bendrea A.D., Lanzalaco S., Franco L., Cianga L., del Valle L.J., Puiggali J., Turon P., Armelin E., Cianga I., Aleman C., Smart design for a flexible, functionalized and electroresponsive hybrid platform based on poly(3,4-ethylenedioxythiophene) derivatives to improve cell viability. *Journal of Materials Chemistry B* 8, **2020**, 8864-8877. DOI: 10.1039/d0tb01259a (**IF: 7.571**); **(8)** Bendrea A.-D., Cianga L., Ailiesei G.-L., Cianga I., Fluorescent EDOT-functionalized Poly-ε-caprolactone: Synthesis, photophysical and self-assembling properties in organic solvents and its serendipitously noticed behaviour in protonated media, *Proceedings*, vol 69 (1), **2021**, 13-14. https://www.mdpi.com/2504-3900/69/1/13; **(9)** Bendrea A.D., Cianga L, Ailiesei G.L., Ursu E.L, Göen Colak D., Cianga I., 3,4-Ethylenedioxythiophene (EDOT) End-group functionalized Poly-ε-caprolactone (PCL): Self-assembly in organic solvents and its coincidentally observed peculiar behavior in thin film and protonated media, *Polymers* 13, **2021**, 2720. DOI: 10.3390/polym13162720 (**IF: 4.967**); **(10)** Bendrea A.-D., Cianga L., Cianga I., Thiophene end-group functionalized oligo(2-methyl-2-oxazoline) as an amphilphilic reactive macromonomer and as a non-conventional intrinsic luminescent material, Proceedings of International Conference, *Progress in Organic and Macromoleculecular Compounds*, pp. 83-84 (**2021**), ISSN 2810-2347; **(11)** Bendrea A.-D., Cianga L., Ailiesei G.L., Goen-Colak D., Popescu I., Cianga I., Thiophene α-chain-end - functionalized oligo(2-methyl-2-oxazoline) as precursor amphiphilic macromonomer for grafted conjugated oligomers / Polymers and as a multifunctional material with relevant properties for biomedical applications, *International Journal of Molecular Sciences*, Accepted 30 of June **2022** (**IF: 6.208**)

A new 3D all-polymer electroactive, flexible interface, constructed in a hierarchical manner, using as a support a film of isotactic polypropylene and as a coating layer a ‘‘molecular composite’’ based on poly(3,4-ethylenedioxythiophene) (PEDOT) backbone and randomly distributed short PCL side chains (PEDOT-g-PCL) was reported by I. Cianga & C. Aleman et all in *J. Mater. Chem. B*, **2020**, 8, 8864. The constructed system has an optimized tissue integration performance with potential applications in bioimplants for tissue regeneration or as soft implantable bioelectronics.

By intelligently combining the components of well-known polymeric biomaterials (PEG and PCL) with a multi-sensitive conjugated polymer (PTh), a biomimetic material was reported by I. Cianga & C. Aleman et all in *Polym. Chem.*, **2019**, 10, 5010–5022. This new material, showing high performances in biomimetic aqueous electrolytes, was used for NADH coenzyme biosensor construction, with a potential impact in the prevention and early diagnosis of neurodegenerative diseases.



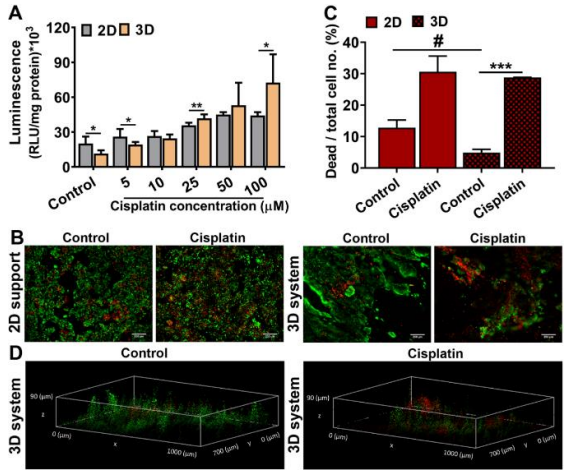
3D all-polymer electroactive, flexible and biocompatible 3D nanoplatform



(Electro) bioactive material used for NADH biosensing

(12) Turtoi M., Anghelache M., Bucatariu S.M., Deleanu M., Voicu G., Safciuc F., Manduteanu I., Fundueanu G., Simionescu M., Calin M., A novel platform for drug testing: Biomimetic three-dimensional hyaluronic acid-based scaffold seeded with human hepatocarcinoma cells, *International Journal of Biological Macromolecules* 185, **2021**, 604-619. DOI: 10.1016/j.ijbiomac.2021.06.174 (**IF: 8.025**).

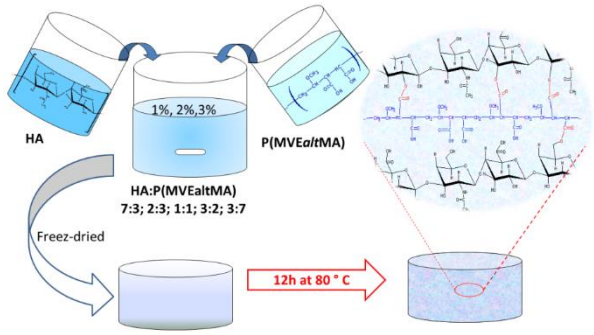
A novel hyaluronic acid (HA)-based 3D cell model (HA^3P50) suitable for chemotherapeutic drug testing on hepatocellular carcinoma was developed. Compared to 2D, the cells grown in the HA^3P50 scaffold proliferate into larger-cellular aggregates that exhibit liver-like functions. Also, growing the cells in the scaffold sensitize the hepatocytes to the anti-tumor effect of cisplatin, by a mechanism involving the activation of ERK/p38α-MAPK and dysregulation of NF-kB/STAT3/Bcl-2 pathways. Moreover, the system can be adapted and employed as experimental platform functioning as a proper tissue/tumor surrogate.



*Cisplatin-induced cytotoxicity in HepG2 cells cultured on 2D support and in HA^3P50 scaffold (3D). HepG2 cells grown on 2D and in 3D systems for 7 days were exposed for 24 hours to 5-100 μM cisplatin or 0.1% DMSO (control cells). (A) The cisplatin cytotoxicity in HepG2 cells was investigated by the release of the adenylate kinase in the culture medium. (B) Live (green)/dead (red) assay of control cells and 25 μM cisplatin-treated HepG2 cells. Scale bar: 200 μm. (C) The percentage of dead/total cell number obtained by live/dead cell assay. (D) 3D reconstruction images of the Z-stacking sections for live/dead assay of control and cisplatin-treated HepG2 cells grown in HA3 P50 scaffold. The results were shown as mean ± SD and analyzed using unpaired two-tailed Student's t-test: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ and # $p < 0.05$.*

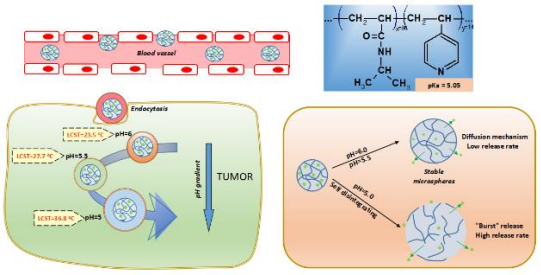
(13) Bucatariu S.M., Constantin M., Varganici C.D., Rusu D., Nicolescu A., Prisacaru I., Carnuta M., Anghelache M., Calin M., Ascenzi P., Fundueanu G., A new sponge-type hydrogel based on hyaluronic acid and poly(methylvinylether-alt-maleic acid) as a 3D platform for tumor cell growth, *International Journal of Biological Macromolecules* 165 (B), **2020**, 2528-2540. DOI: 10.1016/j.ijbiomac.2020.10.095 (**IF: 8.025**)

HepG2 cells cultured for 21 days in the surrogate proliferate to large cellular aggregates and gain liverlike functions such as the improved release of albumin, urea, bile acids, and transaminases, and the enhanced synthesis of CYP7A1. After 7 days, HepG2 cells cultured in scaffold exhibit enhanced chemosensitivity to cisplatin (increased cytotoxicity and DNA fragmentation and rearrangement of the cytoskeleton). The scaffold is hydrolyzed by the enzymatic action of hyaluronidase and is highly absorptive for doxorubicin. The data suggest that the HA/PMVEaltMA) scaffold can be used as an HA-based 3D cell platform for testing the effect of chemotherapeutic drugs on hepatocellular carcinoma. Also, the newly developed HA-based 3D model can be adapted and employed as an experimental platform for drug testing in other pathologies.



Schematic representation of the synthesis steps of surrogate hydrogel based on hyaluronic acid (HA) and poly(methylvinylether-alt-maleic acid) (P(MVEaltMA)) cross-linked by solvent free thermal method.

(14) Constantin M., Bucatariu S., Popescu I., Cosman B., Ascenzi P., Fundueanu G., Intelligent micro-vehicles for drug transport and controlled release to cancer cells, *Reactive and Functional Polymers* 165, **2021**, 104961. DOI: 10.1016/j.reactfunctpolym.2021.104961 (**IF: 4.966**)

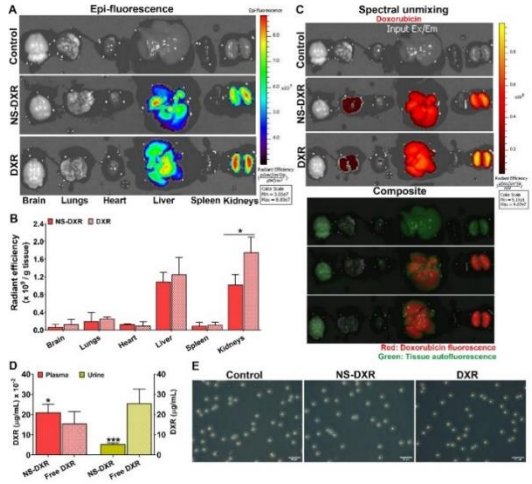


Schematic representation of the poly(N-isopropylacrylamide-co-4-vinylpyridine)-based nano-platforms behaviour after i.v. administration.

Nano-platforms are stable in the blood, accumulate at sites with increased vascular permeability (tumors), where they are internalized by the cancer cells by macropinocytosis, considering their size. In the early and late endosomes (pH: 6.0 –5.5), they are stable but start to disintegrate and release the drug cargo in the lysosomes (pH = 5.0).

(15) Fundueanu G., Constantin M., Turtoi M., Bucatariu S., Cosman B., Anghelache M., Voicu G., Calin M., Bio-responsive carriers for controlled delivery of doxorubicin to cancer cells, *Pharmaceutics* 14, 2022, 865. DOI: 10.3390/pharmaceutics14040865 (**IF: 6.525**).

The bio-responsive poly(N-isopropylacrylamide-co-vinylimidazole) copolymer was synthesized and characterized. The poly(NIPAAm-co-VI)-based nanoparticles are biocompatible and may be introduced as carriers for the antitumoral drug, doxorubicin. The nanoparticles (NS-DXR) might have the potential to deliver DXR to hepatic tumors and, besides, the particulate system can be adapted and endowed with targeting properties by conjugating specific ligands to direct them more efficiently to a certain tumor.



*(**A**) Localization of NS-DXR and free DXR in organs harvested from C57BL/6 mice. The analysis was completed 1 h after the retro-orbital injection of NS-DXR, free DXR, or PBS in mice using the imaging system IVIS Caliper 200, by detection of the DXR fluorescence using the filter set $\lambda_{ex}/\lambda_{em}$: 500 nm/600 nm. (**B**) Quantification of total radiant efficiency in organs using the region-of-interest option of Living Image software. (**C**) Spectral unmixing analysis to delineate the signal specific for DXR fluorescence (red) and tissue autofluorescence (green). (**D**) Quantification of DXR in plasma and urine of mice, 1 h after administration of 3 mg/kg of free DXR or incorporated into NS-DXR, at λ_{ex} = 480 nm and λ_{em} = 590 nm. * $p < 0.05$, *** $p < 0.001$. (**E**) Evaluation of in vivo hemocompatibility by following the erythrocyte aggregation after the administration of NS-DXR and free DXR. Samples from mice who received PBS were considered the negative control. Scale bar: 50 μm.*

(16) Racles C., Zaltariov M.F., Peptanariu D., Vasiliu T., Cazacu M., Functionalized mesoporous silica as doxorubicin carriers and cytotoxicity boosters, *Nanomaterials* 12(11), **2022**, 1823, 1-26. DOI: 10.3390/nano12111823 (**IF: 5.719**)

Mesoporous silica functionalized with thiol groups and, for the first time, its derivative post-modified with glucoside moieties by green thiol-ene photoaddition were prepared and used as carriers for Dox. The physical interactions responsible for the Dox encapsulation were investigated by analytic methods and MD simulations, and were correlated with the high loading efficiency of organo-modified MSNs. The in vitro cytotoxicity was evaluated on NDHF, MeWo and HeLa cell lines by CellTiter-Glo assay, revealing strong cytotoxic effects in all of the loaded silica at low equivalent Dox concentration and selectivity for cancer cells.

(17) Zaltariov M.F., Turtoi M., Peptanariu D., Macsim A.M., Clima L., Cojocaru C., Vornicu N., Ciubotaru B.I., Bargan A., Calin M., Cazacu M., 3 Organosilatrane hanging 5-nitrosalicylaldimine motif: Synthesis, full structural

characterization and a multi-tool approach to assessing its medicinal significance, *European Journal of Medicinal Chemistry*, Under review, 2022 (IF: 7.088)

1-(3-{[(2-Hydroxy-5-nitrophenyl)methylidene]amino}propyl)silatrane, containing two chemical motifs, of interest for medicinal chemistry, silatrane and nitro group, attached in position 5 to salicylaldehyde, coupled in a new structure, through an azomethine moiety, also known as a versatile pharmacophore was isolated for the first time and fully characterized. The cytotoxicity studies on two cancer cell lines (HepG2 and MCF-7), and protein binding ability - with major role in drug ADME, revealed a higher cytotoxic activity on HepG2 and MCF-7 cell lines with higher selectivity on MCF7 cell lines.

VI. The project synopsis

As a new and highly performant scientific domain, nanomedicine runs towards the zenith of real-world applications. Bio-pharma companies have already been mesmerized by the precision and versatility of nanomedicine "tools", and have begun a race headed to „connecting" their biologically- and pharmacologically-active molecules with such tools. Their exhortation: "*We have the molecules, give us the tools!*" addressed to scientists has stimulated inventiveness in the highly confined field of pharmaceutics. Supramolecular chemistry offered one distinctive set of such tools: *the dynamic assembling nano-entities*, including those of *nanoplatforms of assembling-line type*. The Nobel Prize winner Jean-Marie Lehn postulated (in the chapter named *Constitutional Dynamic Chemistry: Bridge from Supramolecular Chemistry to Adaptive Chemistry*, Topics in Current Chemistry, **2012**; Vol. 322: p. 1-32. DOI: 10.1007/128_2011_256.) that non-covalent intermolecular forces convey chemical information contained in the (macro)molecules conformation, and therefore should act as a new dimension, the fifth, in the design and synthesis of functional macromolecular-scale entities. This idea enlivened the 5D-nanoP project.

A class of modern and non-conventional medicines, the inhibitors of carbonic anhydrase enzymes, was chosen as prototypal small-molecular pharmacologic effectors to be vehiculated by means of the nano-scale tool developed during the 5D-nanoP project. A three-sections library of such inhibitors was produced and tested, to cover the antibiotic, the anti-neoplastic, and the anti-obesity effects.

One of the distinctive directions developed into the frame of 5D-nanoP project was the harnessing of the conjugated conductive polymers (CPs) for smart biomedical applications, able to advance the emerging areas of biosynthesis mimicking, and bio-electronic interfacing, which are no longer just futuristic approaches but alternatives to the fastest growing pharmaceuticals. Nanoplatforms based on CPs capable of micellization were produced and tested as assembling-lines and carriers for different low-molecular biological effectors (see ***Figure S.1***). Furthermore, the area of functional polymeric nanoplatforms was extended by silicon-based macromolecular constructs, which were tailored to become triggerable by means of the variation of physiologic factors, like temperature. Hypervalent silicon compounds (silatranes), and organofunctionalized silica provided well adapted characteristics for interfacing with the living-matter (see ***Figure S.2***).

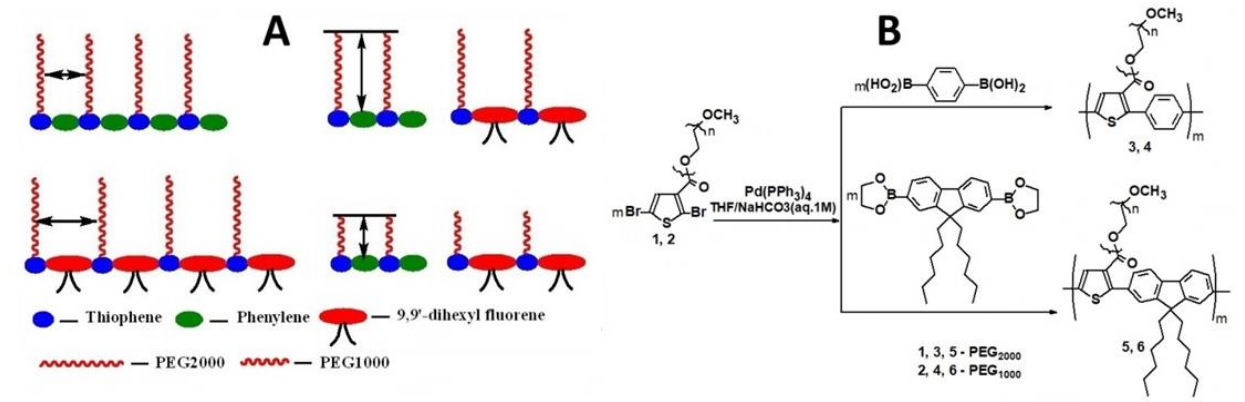


Figure S.1. *(**A**)-Schematic representation of the adopted design criteria for synthesized fluorescent, water-self dispersible conjugated copolymers for the modulation of the micellar nanoplatforms' properties; (**B**)- Synthesis of water self-dispersible conjugated conductive polymers synthesized by Suzuki polycondensation.*

Biologically-active compounds and systems must be extensively tested before their use in clinical trials, or before their applications. This is why, 5D-nanoP project aimed and succeeded to develop *ex vivo* testing systems, of tissues and tumors surrogate types. All the small- and macromolecular compounds, regardless of their functional roles in generating nanoplatforms or in carrying medicines, were tested against the said surrogates.

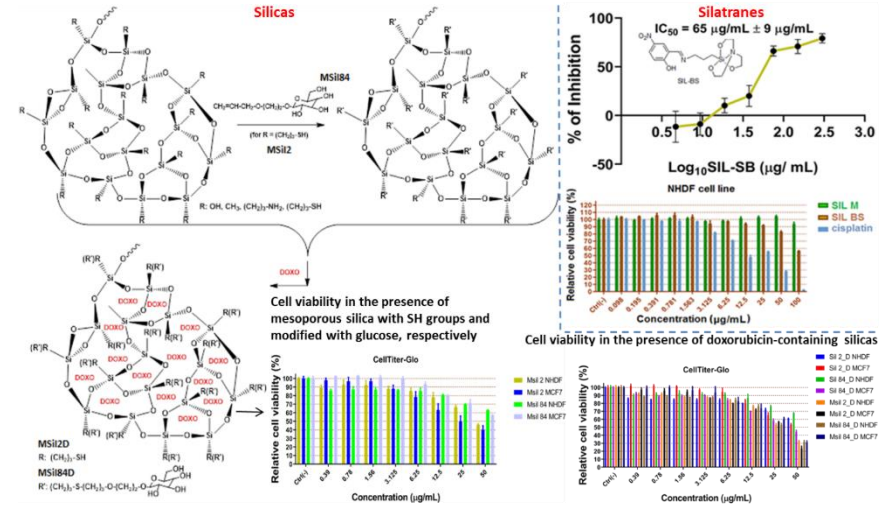


Figure S.2. *Silicas, silatranes, and their mutual derivatives proved to ensure the needed biocompatibility for being accepted as nanoplatforms and carriers for pharmacologically-active small-molecules.*

All the findings into the frame of 5D-nanoP project were supported by computational chemistry approaches, furnished by a solid "*in silico*" team. A significant contribution of this team was related to the elucidation of the mechanisms involved in supramolecular assembling and in active-compounds docking to their targets. ***Figure S.3*** depicts an illustrative example of studying supramolecular functionality.

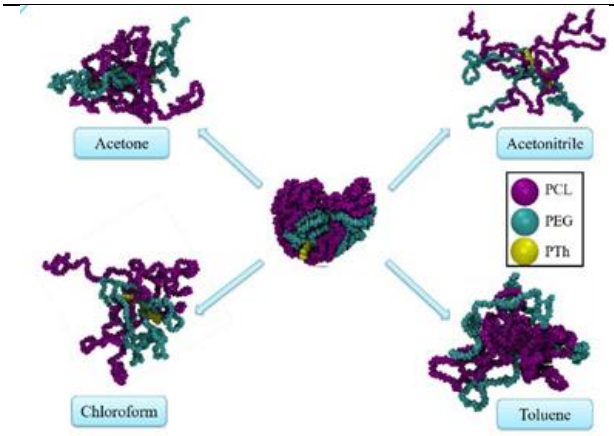


Figure S.3. *Supramolecular conformation control of PTh-g-(PEG-ran-PCL) amphiphilic heterografted polymers by means of organic solvent, as a basis of branches exposure for further reactions or supramolecular interactions.*

DISSEMINATION 2018-2022

103 articles published in ISI journals, 62 participations at international/national conferences, 3 PhD thesis defended, 5 book chapters, meetings between partners, 4 workshops, 9 research stays. (WEB site: https://www.intelcentru.ro/5D-nanoP/).

References

[1] A. Angeli, M. Pinteala, S. S. Maier, S. Del Prete, C. Capasso, B. C. Simionescu, C. T. Supuran, Inhibition of bacterial α-, β- and γ-class carbonic anhydrases with selenazoles incorporating benzenesulfonamide moieties, *Journal of Enzyme Inhibition and Medicinal Chemistry* 34, **2019**, 244-249. DOI: 14756366.2018.1547287

[2] Angeli A., Pinteala M., Maier S.S., del Prete S., Capasso C., Simionescu B.C., Supuran C.T., Inhibition of α-, β-, γ-, δ-, Ɛ- and η- class carbonic anhydrases from bacteria, fungi, algae, diatoms and protozoans with famotidine, *Journal of Enzyme Inhibition and Medicinal Chemistry* 34, **2019**, 644-650. DOI: 10.1080/14756366.2019.1571273

[3] Clima L., Craciun B.F., Angeli A., Petreni A., Bonardi A., Nocentini A., Carta F., Gratteri P., Pinteala M., Supuran C.T., Synthesis, computational studies and assessment of in vitro activity of squalene

derivatives as Carbonic Anhydrase inhibitors, *ChemMedChem* 15, **2020**, 2052-2057. DOI: 10.1002/cmdc.202000500

[4] Angeli A., Pinteala M., Maier S.S., Simionescu B.C., Milaneschi A., Abbas G., del Prete S., Capasso C., Capperucci A., Tanini D., Carta F., Supuran, C. T., Evaluation of thio-and seleno-acetamides bearing benzenesulfonamide as inhibitor of carbonic anhydrases from different pathogenic bacteria, *International Journal of Molecular Science* 21 (2), **2020**, 598. DOI: 10.3390/ijms21020598

[5] Angeli A., Pinteala M., Maier S. S., Toti A., Di Cesare Mannelli L., Ghelardini C., Seleri S, Carta F. Supuran, C. T., Tellurides bearing benzensulfonamide as carbonic anhydrase inhibitors with potent antitumor activity, *Bioorganic & Medicinal Chemistry Letters* 45, **2021**, 128147. DOI: 10.1016/j.bmcl.2021.128147

[6] Molina B.G., Cianga L., Bendrea A.-D., Cianga I., Aleman C., Armelin E., An amphiphilic, heterografted polythiophene copolymer containing biocompatible/ biodegradable side chains for use as an (electro)active surface in biomedical applications, *Polymer Chemistry* **2019**, *10*, 5010–5022. DOI: 10.1039/C9PY00926D

[7] Bendrea A.-D., Cianga L., Cianga I., The simplest is the most sophisticated: A Janus type polythiophene copolymer at work for a biointegrable device, 27th edition of scientific communications "Progress in the field of macromolecular and organic compounds", organized in the frame of Academic Days of Iasi, Romania, 2-4 October **2019** (oral communication).

[8] Racles C., Zaltariov M.F., Peptanariu D., Vasiliu T., Cazacu M., Functionalized mesoporous silica as doxorubicin carriers and cytotoxicity boosters, *Nanomaterials* 12(11), **2022**, 1823. DOI: 10.3390/nano12111823

[9] Molina B.G., Bendrea A.-D., Lanzalaco S., Franco L., Cianga L. del Valle L.J., Puiggali J., Turon P., Armelin E., Cianga I., Aleman C., Smart design for a flexible, functionalized an electroresponsive hybrid platform based on poly(3,4-ethylenedioxythiophene) derivatives to improve cell viability, *Journal of Materials Chemistry B* 8, **2020**, 8864-8877. DOI: 10.1039/D0TB01259A; Bendrea A.D., Cianga L, Ailiesei G.L., Ursu E.L, Göen Colak D., Cianga I., 3,4-Ethylenedioxythiophene (EDOT) End-Group Functionalized Poly-ε-caprolactone (PCL): Self-assembly in organic solvents and its coincidentally observed peculiar behavior in thin film and protonated media, *Polymers* 13, **2021**, art. no. 2720. DOI: 10.3390/polym13162720

[10] David G., Bargan A., Drobota M., Bele A., Rosca I., Comparative investigation of collagen-based hybrid 3D structures for potential biomedical applications, *Materials* 14(12), **2021**, 3313. DOI: 10.3390/ma14123313

[11] Constantin M., Cosman B., Bercea M., Ailiesei G.L., Fundueanu G., Thermosensitive poloxamer-graft-carboxymethyl pullulan: A potential injectable hydrogel for drug delivery, *Polymers* 13, **2021**, 3025. DOI: 10.3390/polym13183025

[12] Bucatariu S.M., Constantin M., Varganici C.D., Rusu D., Nicolescu A., Prisacaru I., Carnuta M., Anghelache M., Calin M., Ascenzi P., Fundueanu G., A new sponge-type hydrogel based on hyaluronic acid and poly(methylvinylether-alt-maleic acid) as a 3D platform for tumor cell growth, *International Journal of Biological Macromolecules* 165 (B), **2020**, 2528-2540. DOI: 10.1016/j.ijbiomac.2020.10.095

[13] Turtoi M., Anghelache M., Bucatariu S.M., Deleanu M., Voicu G., Safciuc F., Manduteanu I., Fundueanu G., Simionescu M., Calin M., A novel platform for drug testing: Biomimetic three-dimensional hyaluronic acid-based scaffold seeded with human hepatocarcinoma cells, *International Journal of Biological Macromolecules* 185, **2021**, 604-619. DOI: 10.1016/j.ijbiomac.2021.06.174

[14] Coroaba A., Isac D.-L., Al-Matarneh C., Vasiliu T., Ibanescu S.-A., Zonda R., Ardeleanu R., Neamtu A., Timpu D., Nicolescu A., Mocci F., Maier S.S., Laaksonen A., Abadie M.J.M., Pinteala M., Probing the supramolecular features via π–π interaction of a di-iminopyrene-di-benzo-18-crown-6-ether compound: Experimental and theoretical study, *RSC Advances* 10, **2020**, 38304-38315. DOI: 10.1039/D0RA06929A.

ANNEX I

Published / Accepted Scientific Papers with acknowledgments at the 5D-nanoP project

2022

1. F. Mocci, L. Engelbrecht, C. Olla, A. Cappai, M.F. Casula, C. Melis, L. Stagi, A. Laaksonen, C. Maria Carbonaro, Carbon nanodots from *in silico* perspective, *Chemical Reviews*, Accepted (2022) (IF: 72.087)

2. Y. Dong, M. Gong, F. Ullah Shah, A. Laaksonen, R. An, X. Ji, Phosphonium-based ionic liquid significantly enhances SERS of cytochrome c on TiO2 nanotube arrays, *ACS Applied Materials & Interfaces* 14(23), 27456-27465 (2022). DOI: https://doi.org/10.1021/acsami.2c05781 (IF: 10.383)

3. Y. Dong, A. Laaksonen, M. Gong, R. An, X. Ji, Selective separation of highly similar proteins on ionic liquid-loaded mesoporous TiO2, *Langmuir* 38, 3202-3211 (2022). DOI: https://doi.org/10.1021/acs.langmuir.1c03277 (IF: 4.331)

4. Z. Zhang, T. Vasiliu, F. Li, A. Laaksonen, X. Zhang, F. Mocci, X. Ji, Novel artificial ionic cofactors for efficient electro-enzymatic conversion of CO2 to formic acid, *Journal of CO2 Utilization* 60, 101978 (2022). DOI: https://doi.org/10.1016/j.jcou.2022.101978 (IF: 8.321)

5. Y. Dong, W. Lin, A. Laaksonen, X. Ji, Complementary powerful techniques for investigating the interactions of proteins with porous TiO2 and its hybrid materials: A tutorial review, *Membranes* 12, 415 (2022). DOI: https://doi.org/10.3390/membranes12040415 (IF: 4.562)

6. F. Li, A. Laaksonen, X. Zhang, X. Ji, Rotten eggs revaluated: Ionic liquids and deep eutectic solvents for removal and utilization of hydrogen sulfide, *Industrial & Engineering Chemistry Research* 61, 2643-2671 (2022). DOI: https://doi.org/10.1021/acs.iecr.1c04142 (IF: 4.326)

7. Y. Wei, Z. Dai, Y. Dong, A. Filippov, X. Ji, A. Laaksonen, F. Ullah Shah, R. An, H. Fuchs, Molecular interactions of ionic liquids with SiO2 surfaces determined from colloid probe atomic force microscopy, *Physical Chemistry Chemical Physics* 24, 12808-12815 (2022). DOI: https://doi.org/10.1039/d2cp00483f (IF: 3.945)

8. Y. Wei, Y. Dong, X. Ji, F. Ullah Shah, A. Laaksonen, R. An, K. Riehemann, Detailing molecular interactions of ionic liquids with charged SiO2 surfaces: A systematic AFM study, *Journal of Molecular Liquids* 350, 118506 (2022). DOI: https://doi.org/10.1016/j.molliq.2022.118506 (IF: 6.633)

9. T. Vasiliu, F. Mocci, A. Laaksonen, L. De Villiers Engelbrecht, S. Perepelytsya, Caging polycations: Effect of increasing confinement on the modes of interaction of spermidine3+ with DNA double helices, *Frontiers in Chemistry* 10, 836994 (2022). DOI: https://doi.org/10.3389/fchem.2022.836994 (IF: 5.545)

10. L. Engelbrecht, X. Ji, Carlo M. Carbonaro, A. Laaksonen, F. Mocci, Excess molar enthalpies of pseudo-binary mixtures of a choline chloride-based deep eutectic solvent with water or methanol: An MD computer simulation study, Submitted to*: Frontiers in Chemistry* (2022). (IF: 5.545)

11. A.R. Petrovici, M. Silion, N. Simionescu, R. Kallala, M. Pinteala, S.S. Maier, Quantification of low amounts of zoledronic acid by HPLC-ESI-MS analysis: Method development and validation, *International Journal of Molecular Sciences* 23, 5944 (2022). DOI: https://doi.org/10.3390/ijms23115944 (IF: 6.208)

12. G. Voicu, D. Rebleanu, C.A. Mocanu, G. Tanko, I. Droc, C.M. Uritu, M. Pinteala, I. Manduteanu, M. Simionescu, M. Calin, VCAM-1 targeted lipopolyplexes as vehicles for efficient delivery of shRNA-Runx2 to osteoblast-differentiated valvular interstitial cells; Implications in calcific valve disease treatment, *International Journal of Molecular Sciences* 23, 3824 (2022). DOI: https://doi.org/10.3390/ijms23073824 (IF: 6.208)

13. A. Angeli, V. Kartsev, A. Petrou, B. Lichitsky, A. Komogortsev, M. Pinteala, A. Geronikaki, C.T. Supuran, Pyrazolo[4,3-c]pyridine sulfonamides as Carbonic Anhydrase inhibitors: Synthesis, biological and *in silico* studies, *Pharmaceuticals*, 15, 316 (2022). DOI: https://doi.org/10.3390/ph15030316 (IF: 5.215)

14. O.E. Carp, M. Pinteala, A. Arvinte, Innovative non-enzymatic electrochemical quantification of cholesterol, *Sensors* 22, 828 (2022). DOI: https://doi.org/10.3390/s22030828 (IF: 3.847)

15. G. Fundueanu, M. Constantin, M. Turtoi, S. Bucatariu, B. Cosman, M. Anghelache, G. Voicu, M. Calin, Bio-responsive carriers for controlled delivery of doxorubicin to cancer cells, *Pharmaceutics* 14, 865 (2022). DOI: https://doi.org/10.3390/pharmaceutics14040865 (IF: 6.525)

16. M. Constantin, B. Cosman, P. Ascenzi, B.C. Simionescu, G. Fundueanu, New chromatographic insights on drug: cyclodextrin inclusion complexes and their potential use in drug delivery, *International Journal of Biological Macromolecules*, Submitted (2022). (IF: 8.025)

17. C. Racles, M.F. Zaltariov, D. Peptanariu, T. Vasiliu, M. Cazacu, Functionalized mesoporous silica as doxorubicin carriers and cytotoxicity boosters, *Nanomaterials* 12, 1823, (2022). DOI: https://doi.org/10.3390/nano12111823 (IF: 5.719)

18. M. Turtoi, M. Anghelache, A.A. Patrascu, M. Deleanu, G. Voicu, M. Raduca, F. Safciuc, I. Manduteanu, M. Calin, D.-L. Popescu, Antitumor properties of a new macrocyclic tetranuclear oxidovanadium(V) complex with 3-methoxysalicylidenvaline ligand, *Biomedicines* 10, 1217 (2022). DOI: https://doi.org/10.3390/biomedicines10061217 (IF: 4.757)
19. B.I. Ciubotaru, M.F. Zaltariov, C. Tugui, I.E. Stoleru, D. Peptanariu, G.T. Stiubianu, N. Vornicu, M. Cazacu, Silicones with different crosslinking patterns: assessment from the perspective of their suitability for biomaterials, *Surfaces and Interfaces*, Accepted (2022) (IF: 6.137)
20. M.F. Zaltariov, M. Turtoi, D. Peptanariu, A.M. Macsim, L. Clima, C. Cojocaru, N. Vornicu, B.I. Ciubotaru, A. Bargan, M. Calin, M. Cazacu, Organosilatrane hanging 5-nitrosalicylaldimine motif: Synthesis, full structural characterization and a multi-tool approach to assessing its medicinal significance, *European Journal of Medicinal Chemistry*, Under review (2022) (IF: 7.088)
21. A.-D. Bendrea, L. Cianga, G.L. Ailiesei, D. Goen-Colak, I. Popescu, I. Cianga, Thiophene α-chain-end - functionalized oligo(2-methyl-2-oxazoline) as precursor amphiphilic macromonomer for grafted conjugated oligomers / polymers and as a multifunctional material with relevant properties for biomedical applications, *International Journal of Molecular Sciences*, revised version under review 22.06.2022, manuscript ID ijms-1778522 (2022) (IF: 6.208)
22. S. Cibotaru, V. Nastasa, A.-I. Sandu, A.-C. Bostanaru, M. Mares, L. Marin, Pegylation of phenothiazine – A synthetic route towards potent anticancer drugs, *Journal of Advanced Research* 37, 279-290 (2022). DOI: https://doi.org/10.1016/j.jare.2021.07.003 (IF: 12.822)
23. C. Stavarache, A. Nicolescu, C. Duduianu, G. L. Ailiesei, M. Balan-Porcarasu, M. Cristea, A.-M. Macsim, O. Popa, C. Stavarache, A. Hirtopeanu, L. Barbes, R. Stan, H. Iovu, C. Deleanu, A real-life reproducibility assessment for NMR metabolomics, *Diagnostics* 12, 559 (2022). DOI: https://doi.org/10.3390/diagnostics12030559 (IF: 3.992)
24. E. Papadopoulou, A. Nicolescu, L.S. Haug, T. Husøy, C. Deleanu, H. Dirven, B. Lindeman, Lipoprotein profiles associated with exposure to poly- and perfluoroalkyl substances (PFASs) in the EuroMix human biomonitoring study, *Environmental Pollution*, In Press / Early View (2022). DOI: https://doi.org/10.1016/j.envpol.2022.119664 (IF: 9.988)
25. L.-A. Stanciulescu, A. Scafa, C. Duduianu, R. Stan, A. Nicolescu, C. Deleanu, M. Dorobanțu, Lipoprofiling assessed by NMR spectroscopy in patients with acute coronary syndromes. Is the need for fasting prior to sampling?, *Diagnostics*, Accepted (2022) (IF: 3.992)
26. F.L. Barroso da Silva, C. Corrêa Giron, A. Laaksonen, Electrostatic features for the receptor binding domain of SARS-COV-2 wildtype and its variants. Compass to the severity of the future variants with the charge-rule, BioRxiv, June 17, 2022 - https://doi.org/10.1101/2022.06.16.496458 - To be published in *Journal of Physical Chemistry B* (IF: 3.466)
27. A. Neamtu, F. Mocci, A. Laaksonen, F.L. Barroso da Silva, Towards an optimal monoclonal antibody with higher binding affinity to the receptor-binding domain of SARS-CoV-2 spike proteins from different variants, BioRxiv Jan 5, 2022, 1-59. DOI: https://doi.org/10.1101/2022.01.04.474958 - To be published in *RSC Medicinal Chemistry* (IF: 3.47)
28. C. Correa Giron, A. Laaksonen, F. Luis Barroso da Silva, Differences between Omicron SARS-CoV-2 RBD and other variants in their ability to interact with cell receptors and monoclonal antibodies, BioRxiv, Jan 31 2022, 1-69. DOI: https://doi.org/10.1101/2022.01.29.478316 - To be published in *Journal of Biomolecular Structure & Dynamics* (IF: 5.235)

2021

29. M. Turtoi, M. Anghelache, S.M. Bucatariu, M. Deleanu, G. Voicu, F. Safciuc, I. Manduteanu, G. Fundueanu, M. Simionescu, M. Calin, A novel platform for drug testing: Biomimetic three-dimensional hyaluronic acid-based scaffold seeded with human hepatocarcinoma cells, *International Journal of Biological Macromolecules* 185, 604-619 (2021). DOI: https://doi.org/10.1016/j.ijbiomac.2021.06.174 (IF: 8.025)
30. I. Popescu, M. Turtoi, D.M. Suflet, M.V. Dinu, R.N. Darie-Nita, M. Anghelache, M. Calin, M. Constantin, Alginate/poloxamer hydrogel obtained by thiol-acrylate photopolymerization for the alleviation of the inflammatory response of human keratinocytes, *International Journal of Biological Macromolecules* 180, 418-431 (2021). DOI: https://doi.org/10.1016/j.ijbiomac.2021.03.082 (IF: 8.025)
31. M. Turtoi, M. Anghelache, A.A. Patrascu, C. Maxim, I. Manduteanu, M. Calin, D.L. Popescu, Synthesis, characterization, and *in vitro* insulin-mimetic activity evaluation of valine Schiff base coordination compounds of oxidovanadium(V). *Biomedicines* 9, 562 (2021). DOI: https://doi.org/10.3390/biomedicines9050562 (IF: 4.757)

32. C.A. Mocanu, E.V. Fuior, G. Voicu, D. Rebleanu, F. Safciuc, M. Deleanu, I.M. Fenyo, V. Escriou, I. Manduteanu, M. Simionescu, M. Calin, P-selectin targeted RAGE-shRNA lipoplexes alleviate atherosclerosis-associated inflammation, *Journal of Controlled Release* 338, 754-772 (2021). DOI: https://doi.org/10.1016/j.jconrel.2021.09.012 (IF: 11.467)
33. A.-M. Macsim, E. Georgescu, F. Georgescu, P. Filip, A. Nicolescu, C. Deleanu, Benzimidazolium salts as starting materials or intermediates in 1,3-dipolar cycloadditions, *Monatshefte für Chemie* 152, 845-852 (2021). DOI: https://doi.org/10.1007/s00706-021-02795-7 (IF: 1.613)
34. V. Cozma, I. Rosca, L. Radulescu, C. Martu, V. Nastasa, C.-D. Varganici, E.-L.Ursu, F. Doroftei, M Pinteala, C. Racles, Antibacterial polysiloxane polymers and coatings for cochlear implants, *Molecules* 26(16), 4892 (2021). DOI: https://doi.org/10.3390/molecules26164892 (IF: 4.927)
35. A. R. Petrovici, N. Simionescu, A. I. Sandu, V. Paraschiv, M. Silion, M. Pinteala, New insights on hemp oil enriched in Cannabidiol: Decarboxylation, antioxidant properties and *in vitro* anticancer effect, *Antioxidants* 10, 738 (2021). DOI: https://doi.org/10.3390/antiox10050738 (IF: 7.675)
36. N.B. Tudorachi, E.E. Totu, A. Fifere, V Ardeleanu, V. Mocanu, C. Mircea, I. Isildak, K. Smilkov, E.M. Carausu, The implication of reactive oxygen species and antioxidants in knee osteoarthritis, *Antioxidants* 10, 985 (2021). DOI: https://doi.org/10.3390/antiox10060985 (IF: 7.675)
37. M.-F. Zaltariov, D. Filip, D. Macocinschi, C. Ibanescu, M. Danu, L. Sacarescu, Self-assembly and rheological behavior of chloramphenicol-based poly(ester ether)urethanes, *Journal of Polymer Research* 28, 190 (2021). DOI: https://doi.org/10.1007/s10965-021-02545-7 (IF: 3.061)
38. G. David, A. Bargan, M. Drobota, A. Bele, I. Rosca, Comparative investigation of collagen-based hybrid 3D structures for potential biomedical applications, *Material*s 14, 3313 (2021). DOI: https://doi.org/10.3390/ma14123313 (IF: 3.748)
39. A.L. Chibac-Scutaru, C. Cojocaru, Gh. Roman, P. Samoila, G. Sacarescu, M. Simionescu, L. Sacarescu, Synthesis of benzaldehyde-grafted polysilane: A highly stable and selective "turn-on" fluorescent sensor for cytosine, *Journal of Molecular Liquids* 326, 115300 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.115300 (IF: 6.633)
40. E. Tarabukina, V. Harabagiu, G. Fundueanu, M. Constantin, A. Filippov, Thermo- and pH-responsive copolymer of N-isopropylacrylamide with acryloylvaline: synthesis and properties in aqueous solutions, *Journal of Polymer Research* 28, 155 (2021). DOI: https://doi.org/10.1007/s10965-021-02515-z (IF: 3.061)
41. M. Constantin, B. Cosman, M. Bercea, G.L. Ailiesei, G. Fundueanu, Thermosensitive poloxamer-graft-carboxymethyl pullulan: A potential injectable hydrogel for drug delivery, *Polymers* 13, 3025 (2021). DOI: https://doi.org/10.3390/polym13183025 (IF: 4.967)
42. M. Constantin, S. Bucatariu, I. Popescu, B. Cosman, P. Ascenzi, G. Fundueanu, Intelligent micro-vehicles for drug transport and controlled release to cancer cells, *Reactive and Functional Polymers* 165, 104961 (2021). DOI: https://doi.org/10.1016/j.reactfunctpolym.2021.104961 (IF: 4.966)
43. A. Angeli, M. Pinteala, S.S. Maier, A. Toti, L. Di Cesare Mannelli, C. Ghelardini, S. Selleri, F. Carta, C.T. Supuran, Tellurides bearing benzensulfonamide as carbonic anhydrase inhibitors with potent antitumor activity, *Bioorganic & Medicinal Chemistry Letters* 45, 128147 (2021). DOI: https://doi.org/10.1016/j.bmcl.2021.128147 (IF: 2.94)
44. A. Angeli, M. Ferraroni, A.A. Da'dara, S. Selleri, M. Pinteala, F. Carta, P. J. Skelly, C.T. Supuran, Structural insights into *Schistosoma mansoni* Carbonic Anhydrase (SmCA) inhibition by selenoureido-substituted benzenesulfonamides, *Journal of Medicinal Chemistry* 64, 10418-10428 (2021). DOI: https://doi.org/10.1021/acs.jmedchem.1c00840 (IF: 8.039)
45. T. Vasiliu, B.F. Craciun, A. Neamtu, L. Clima, D.L. Isac, S.S. Maier, M. Pinteala, F. Mocci, A. Laaksonen, *In silico* study of PEI-PEG-squalene-dsDNA polyplex formation: the delicate role of the PEG length in the binding of PEI to DNA, *Biomaterials Science* 9, 6623-6640 (2021). DOI: https://doi.org/10.1039/d1bm00973g (IF: 7.59)
46. A.D. Bendrea, L Cianga, G.L. Ailiesei, E.L Ursu, D. Göen Colak, I. Cianga, 3,4-Ethylenedioxythiophene (EDOT) end-group functionalized poly-ε-caprolactone (PCL): Self-assembly in organic solvents and its coincidentally observed peculiar behavior in thin film and protonated media, *Polymers* 13, 2720 (2021). DOI: https://doi.org/10.3390/polym13162720 (IF: 4.967)
47. D. Filip, D. Macocinschi, C.G. Tuchilus, M.F. Zaltariov, C.D. Varganici, Synthesis, characterization of erythromycin propionate core-based star poly(ether urethane)s and their antibacterial properties, *Macromolecular Research* 29, 613–624 (2021). DOI: https://doi.org/10.1007/s13233-021-9069-5 (IF: 2.127)

48. F. Li, F. Mocci, X. Zhang, X. Ji, A. Laaksonen. Ionic liquids for CO2 electrochemical reduction, *Chinese Journal of Chemical Engineering* 31, 75-93 (2021). DOI: https://doi.org/10.1016/j.cjche.2020.10.029 (IF: 3.898)
49. Q. Gao, Y. Zhang, A. Laaksonen, X. Ji, S. Zhao, Y. Chen, X. Lu, Effect of dimethyl carbonate on the behavior of water confined in carbon nanotube, *Chinese Journal of Chemical Engineering* 31, 177-185 (2021). DOI: https://doi.org/10.1016/j.cjche.2020.10.041 (IF: 3.898)
50. Y. Dong, F. Huo, A. Laaksonen, Detecting confined fluid behavior by SFA: Past, present, and future, *Green Energy & Environment* 6, 167-168 (2021). DOI: https://doi.org/10.1016/j.gee.2020.08.002 (IF: 12.781)

2020

51. E. L. Ursu, G. Gavril, S. Morariu. M. Pinteala, M. Barboiu, A. Rotaru, Single-walled carbon nanotubes-G-quadruple hydrogel nanocomposite matrixes for cell support applications, *Materials Science & Engineering C-Materials for Biological Applications* 111, 110800 (2020). DOI: https://doi.org/10.1016/j.msec.2020.110800 (IF: 8.457)
52. L. Clima, B. F. Craciun, A. Angeli, A. Petreni, A. Bonardi, A. Nocentini, F. Carta, P. Gratteri, M. Pinteala, C. T. Supuran, Synthesis, computational studies and assessment of in vitro inhibitory activity of squalene derivatives as carbonic anhydrase inhibitors, *ChemMedChem* 15, 2052 (2020). DOI: https://doi.org/10.1002/cmdc.202000500 (IF: 3.54)
53. A. Angeli, M. Pinteala, S.S. Maier, B.C. Simionescu, A. Milaneschi, G. Abbas, S. del Prete, C. Capasso, A. Capperucci, D. Tanini, F. Carta, C.T. Supuran, Evaluation of thio- and seleno-acetamides bearing benzenesulfonamide as inhibitor of carbonic anhydrases from different pathogenic bacteria, *International Journal of Molecular Sciences* 21, 598 (2020). DOI: https://doi.org/10.3390/ijms21020598 (IF: 6.208)
54. A. Angeli, M. Ferraroni, M. Pinteala, S.S. Maier, B.C. Simionescu, F. Carta, S. Del Prete, C. Capasso, C.T. Supuran, Crystal structure of a tetrameric type II β-carbonic anhydrase from the pathogenic bacterium Burkholderia pseudomallei, *Molecules* 25, 2269 (2020). DOI: https://doi.org/10.3390/molecules25102269 (IF: 4.927)
55. D. Macocinschi, D. Filip, B.-I. Ciubotaru, R. P. Dumitriu, C. D. Varganici, M.-F. Zaltariov, Blends of sodium deoxycholate-based poly(ester ether)urethane ionomer and hydroxypropyl cellulose with mucosal adhesiveness, *International Journal of Biological Macromolecules* 162, 1262-1275 (2020). DOI: https://doi.org/10.1016/j.ijbiomac.2020.06.191 (IF: 8.025)
56. S. Shova, A. Vlad, M. Damoc, V. Tiron, M. Dascalu, G. Novitchi, C. Ursu, M. Cazacu, Nanoscale coordination polymer of dimanganese(II) as infinite, flexible nano-sheets with photo-switchable morphology, *European Journal of Inorganic Chemistry* 8, 2043-2054 (2020). DOI: https://doi.org/10.1002/ejic.202000098 (IF: 2.551)
57. S. Shova, V. Tiron, A. Vlad, G. Novitchi, D. G. Dumitrescu, M. Damoc, M.-F. Zaltariov, M. Cazacu, Permethylated dinuclear Mn(III) coordination nanostructure with stripe-ordered magnetic domains, *Applied Organometallic Chemistry* 34, e5957 (2020). DOI: https://doi.org/10.1002/aoc.5957 (IF: 4.072)
58. S. P. Gavrish, S. Shova, M. Cazacu, Y. D. Lampeka, Crystal structure of the one-dimensional coordination polymer formed by the macrocyclic [Ni(cyclam)]2+ cation and the dianion of diphenylsilanediylbis(4-benzoic acid). *Acta Crystallographica Section E-Crystallographic Communications* 76, 929-932 (2020). DOI: https://doi.org/10.1107/S2056989020006544 (IF: 0.347)
59. B. G. Molina, A. D. Bendrea, S. Lanzalaco, L. Franco, L. Cianga, L. J. del Valle, J. Puiggali, P. Turon, E. Armelin, I. Cianga, C. Aleman, Smart design for a flexible, functionalized and electroresponsive hybrid platform based on poly(3,4-ethylenedioxythiophene) derivatives to improve cell viability, *Journal of Materials Chemistry B* 8, 8864-8877 (2020). DOI: https://doi.org/10.1039/d0tb01259a (IF: 7.571)
60. S. Cibotaru, A.-I. Sandu, D. Belei, L. Marin, Water soluble PEGylated phenothiazines as valuable building blocks for bio-materials, *Materials Science & Engineering C-Materials for Biological Applications* 116, 111216 (2020). DOI: https://doi.org/10.1016/j.msec.2020.111216 (IF: 8.457)
61. S. M. Bucatariu, M. Constantin, C. D. Varganici, D. Rusu, A. Nicolescu, I. Prisacaru, M. Carnuta, M. Anghelache, M. Calin, P. Ascenzi, G. Fundueanu, A new sponge-type hydrogel based on hyaluronic acid and poly(methylvinylether-alt-maleic acid) as a 3D platform for tumor cell growth, *International Journal of Biological Macromolecules* 165, 2528-2540 (2020). DOI: https://doi.org/10.1016/j.ijbiomac.2020.10.095 (IF: 8.025)
62. D. M. Suflet, I. Popescu, A. I. Prisacaru, I. M. Pelin, Synthesis and characterization of curdlan-phosphorylated curdlan based hydrogels for drug release, *International Journal of Polymeric Materials and Polymeric Biomaterials* 1-10 (2020). DOI: https://doi.org/10.1080/00914037.2020.1765360 (IF: 3.221)

63. D. Timpu, L. Sacarescu, T. Vasiliu, M. V. Dinu, G. David, Surface cationic functionalized nano-hydroxyapatite – Preparation, characterization, effect of coverage on properties and related applications, *European Polymer Journal* 132, 109759 (2020). DOI: https://doi.org/10.1016/j.eurpolymj.2020.109759 (IF: 5.546)
64. C. Cojocaru, L. Clima, Polymer assisted ultrafiltration of AO7 anionic dye from aqueous solutions: Experimental design, multivariate optimization, and molecular docking insights, *Journal of Membrane Science* 604, 118054 (2020). DOI: https://doi.org/10.1016/j.memsci.2020.118054 (IF: 10.53)
65. A.L. Chibac-Scutaru, C. Cojocaru, A. Coroaba, Gh. Roman, G. Sacarescu. M. Simionescu, L. Sacarescu, Nano-assembled oligosilane-pyrazoline structures and their optical properties, *Journal of Molecular Liquids* 303, 112657 (2020). DOI: https://doi.org/10.1016/j.molliq.2020.112657 (IF: 6.633)
66. A. Coroaba, D.-L. Isac, C. Al-Matarneh, T. Vasiliu, S.-A. Ibanescu, R. Zonda, R. Ardeleanu, A. Neamtu, D. Timpu, A. Nicolescu, F. Mocci, S. S. Maier, A. Laaksonen, M. J. M. Abadie, M. Pinteala, Probing the supramolecular features via π–π interaction of a di-iminopyrene-di-benzo-18-crown-6-ether compound: experimental and theoretical study, *RSC Advances* 10, 38304-38315 (2020). DOI: https://doi.org/10.1039/D0RA06929A (IF: 4.036)
67. Y. Sun, A. Laaksonen, X. Lu, X. Ji, How to detect possible pitfalls in ePC-SAFT modelling. 2. Extension to binary mixtures of 96 ionic liquids with CO2, H2S, CO, O2, CH4, N2, and H, *Industrial & Engineering Chemistry Research* 59, 21579-21591 (2020). DOI: https://doi.org/10.1021/acs.iecr.0c04485 (IF: 4.326)
68. Y. A. Dmitriev, A. Laaksonen, N. P. Benetis, H/D isotope effect observed in the isotropic Fermi contact interaction of formyl radical: Experimental and theoretical analysis of the inter- and intra-molecular dynamics, *AIP Advances* 10, 125309 (2020). DOI: https://doi.org/10.1063/5.0027835 (IF: 1.697)
69. Y. Dong, X. Ji, A. Laaksonen, W. Cao, H. He, X. Lu, Excellent protein immobilization and stability on heterogeneous C-TiO2 hybrid nanostructures: A single protein AFM study, *Langmuir* 36, 9323-9332 (2020). DOI: https://doi.org/10.1021/acs.langmuir.0c01942 (IF: 4.331)
70. Q. Gao, Y. Zhang, S. Xu, A. Laaksonen, Y. Zhu, X. Ji, X. Lu, Physicochemical properties and structure of fluid at nano-/ micro-interface: Progress in simulation and experimental study, *Green Energy & Environment* 5, 274-285 (2020). DOI: https://doi.org/10.1016/j.gee.2020.07.013 (IF: 12.781)
71. Q. Gao, N. Wu, Y. Qin, A. Laaksonen, Y. Zhu, X. Ji, X. Lu, Molecular insight into wetting behavior of deep eutectic solvent droplets on ionic substrates: A molecular dynamics study, *Journal of Molecular Liquids* 319, 114298 (2020). DOI: https://doi.org/10.1016/j.molliq.2020.114298 (IF: 6.633)
72. C. Correa Girona, A. Laaksonen, F. L, Barroso da Silva. On the interactions of the receptor-binding domain of SARS-CoV-1 and SARS-CoV-2 spike proteins with monoclonal antibodies and the receptor ACE2, *Virus Research* 285, 198021 (2020). DOI: https://doi.org/10.1016/j.virusres.2020.198021 (IF: 6.286)
73. S.-C. Yang, B. Li, Y.-L. Zhu, A. Laaksonen, Y.-L. Wang, The ENUF method - Ewald summation based on non-uniform Fast Fourier Transform: implementation, parallelization, and application, *Journal of Computational Chemistry* 41, 2316-2335 (2020). DOI: https://doi.org/10.1002/jcc.26395 (IF: 3.672)
74. Y. Sun, Z. Zuo, A. Laaksonen, X. Lu, X. Ji, How to detect possible pitfalls in ePC-SAFT modelling: Extension to ionic liquids, *Fluid Phase Equilibria* 519, 112641 (2020). DOI: https://doi.org/10.1016/j.fluid.2020.112641 (IF: 2.745)
75. H. Wang, Y. Liu, A. Laaksonen, A. Krook-Riekkola, Z. Yang, X. Lu, X. Ji, Carbon recycling – an immense resource and key to a smart climate engineering: A survey of technologies, cost and impurity impact, *Renewable & Sustainable Energy Reviews* 131, 110010 (2020). DOI: https://doi.org/10.1016/j.rser.2020.110010 (IF: 16.799)
76. Y.-L. Wang, B. Li, S. Sarman, F. Mocci, Z.-Y. Lu, J. Yuan, A. Laaksonen, M. D. Fayer, Microstructural and dynamical heterogeneities in ionic liquids, *Chemical Reviews* 120, 5798-5877 (2020). DOI: https://doi.org/10.1021/acs.chemrev.9b00693 (IF: 72.087)
77. H.-W. Pei, B. Li, A. Laaksonen, Y.-L. Wang, How molecular chiralities of bis(mandelato)borate anions affect their binding structures with alkali metal ions and microstructural properties in tetraalkylphosphonium ionic liquids, *Frontiers in Chemistry* 8, 65 (2020). DOI: https://doi.org/10.3389/fchem.2020.00065 (IF: 5.545)
78. Y.-L. Wang, B. Li, J. Yuan, A. Laaksonen, The Effect of phenyl substitutions on microstructures and dynamics of tetraalkylphosphonium bis(trifluoromethylsulfonyl)imide ionic liquids, *ChemPhysChem* 21, 1202-1214 (2020). DOI: https://doi.org/10.1002/cphc.201901206 (IF: 3.52)
79. A. Nicolescu, D. Blanita, C. Boiciuc, V. Hlistun, M. Cristea, D. Rotaru, L. Pinzari, A. Oglinda, A. Stamati, I. Tarcomnicu, A. Tutulan-Cunita, D. Stambouli, S. Gladun, N. Revenco, N. Usurelu, C. Deleanu,

Monitoring methylmalonic aciduria by NMR urinomics. *Molecules* 25, 5312 (2020). DOI: https://doi.org/10.3390/molecules25225312 (IF: 4.927)

80. A. Nicolescu, E. Georgescu, F. Dumitrascu, F. Georgescu, F. Teodorescu, C. Draghici, M.R. Caira, C. Deleanu, Exocyclic enamine of pyrrolo[1,2-a]quinoxalines generated by 1,3-dipolar cycloaddition reactions of benzimidazolium ylides to activated alkynes, *Revista de Chimie* 71(3), 197-209 (2020). DOI: https://doi.org/10.37358/RC.20.3.7989 (IF: 1.755)

81. R. Vulturar, A. Chis, M. Baizat, A. Cozma, R. Suharoschi, A. Nicolescu, C. Deleanu, A severe neonatal argininosuccinic aciduria case investigated by 1H NMR spectroscopy, *Revista de Chimie* 71(3), 210-218 (2020). DOI: https://doi.org/10.37358/RC.20.3.7990 (IF: 1.755)

82. E. Georgescu, F. Georgescu, F. Dumitrascu, C. Draghici, A. Nicolescu, D. Marinescu, C. Deleanu, Microwave-assisted multicomponent synthesis of benzo[f]pyrrolo[1,2-a]quinoline derivatives, *Revue Roumaine de Chimie* 65(1), 97-102 (2020). DOI: https://doi.org/10.33224/rrch.2020.65.1.11 (IF: 0.41)

2019

83. Y. Dong, X. Ji, A. Laaksonen, W. Cao, R. An, L. Lu, X. Lu, Determination of the small amount of proteins interacting with TiO_2 nanotubes by AFM-measurement, *Biomaterials* 192, 368-376 (2019). DOI: https://doi.org/10.1016/j.biomaterials.2018.11.013 (IF: 15.304)

84. A. Angeli, S. Del Prete, M. Pinteala, S. S. Maier, W. A. Donald, B. C. Simionescu, C. Capasso, C. T. Supuran, The first activation study of the β-carbonic anhydrases from the pathogenic bacteria *Brucella suis* and *Francisella tularensis* with amines and amino acids, *Journal of Enzyme Inhibition and Medicinal Chemistry* 34, 1178-1185 (2019). DOI: https://doi.org/10.1080/14756366.2019.1630617 (IF: 5.756)

85. A. Angeli, M. Pinteala, S. S. Maier, S. Del Prete, C. Capasso, B. C. Simionescu, C. T. Supuran, Inhibition of bacterial α-, β- and γ-class carbonic anhydrases with selenazoles incorporating benzenesulfonamide moieties, *Journal of Enzyme Inhibition and Medicinal Chemistry* 34, 244-249 (2019). DOI: https://doi.org/10.1080/14756366.2018.1547287 (IF: 5.756)

86. A. Angeli, M. Pinteala, S. S. Maier, S. Del Prete, C.Capasso, B. C. Simionescu, C. T. Supuran, Inhibition of α-, β-, γ-, δ-, ζ- and η- class carbonic anhydrases from bacteria, fungi, algae, diatoms and protozoans with famotidine, *Journal of Enzyme Inhibition and Medicinal Chemistry* 34, 644-650 (2019). DOI: https://doi.org/10.1080/14756366.2019.1571273 (IF: 5.756)

87. D. L. Isac, A. Airinei, D. Maftei, I. Humelnicu, F. Mocci, A. Laaksonen, M. Pinteala, On the charge-transfer excitations in azobenzene maleimide compounds. A theoretical study, *Journal of Physical Chemistry A* 123, 5525-5536 (2019). DOI: https://doi.org/10.1021/acs.jpca.9b02082 (IF: 2.944)

88. S. Perepelytsya, J. Ulicny, A. Laaksonen, F. Mocci, Pattern preferences of DNA nucleotide motifs by polyamine putrescine^{2+}, spermidine^{3+} and spermine^{4+}, *Nucleic Acids Research* 47, 6084-6097 (2019). DOI: https://doi.org/10.1093/nar/gkz434 (IF: 19.16)

89. N. Marangoci, D. Timpu, A. Corciova, C. Mircea, A.-R. Petrovici, A. Nicolescu, E.-L. Ursu, V. Nastasa, A.C. Bostanaru, M. Mares, M. Pertea, M. Pinteala, β-Cyclodextrin as a functional excipient used for enhancing the diminazene aceturate bioavailability, *Pharmaceutics* 11, 295-311 (2019). DOI: https://doi.org/10.3390/pharmaceutics11060295 (IF: 6.525)

90. S. Liang, K. W. Hall, A. Laaksonen, Z. Zhang, P. G. Kusalik, Characterizing key features in the formation of ice and gas hydrate systems, *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences* 377, 20180167/1-28 (2019). DOI: https://doi.org/10.1098/rsta.2018.0167 (IF: 4.019)

91. S. Sarman, Y. L. Wang, A. Laaksonen, Shear flow simulations of smectic liquid crystals based on the Gay-Berne fluid and the soft sphere string-fluid, *Physical Chemistry Chemical Physics* 21, 292-305 (2019). DOI: https://doi.org/10.1039/C8CP05077E (IF: 3.945)

92. C. Racles, M. F. Zaltariov, M. Silion, A. M. Maxim, V. Cozan, Photo-oxidative degradation of doxorubicin with siloxane MOFs by exposure to daylight, *Environmental Science and Pollution Research* 26, 19684-19696 (2019). DOI: https://doi.org/10.1007/s11356-019-05288-7 (IF: 5.19)

93. I.-A. Turin-Moleavin, A. Fifere, A.-L. Lungoci, I. Rosca, A. Coroaba, D. Peptanariu, V. Nastasa, S.-A. Pasca, A.-C. Bostanaru, M. Mares, M. Pinteala, *In vitro* and *in vivo* antioxidant activity of the new magnetic-cerium oxide nanoconjugates, *Nanomaterials* 9, 1565 (2019). DOI: https://doi.org/10.3390/nano9111565 (IF: 5.719)

94. B. G. Molina, L. Cianga, A.-D. Bendrea, I. Cianga, C. Aleman, E. Armelin, An amphiphilic, heterografted polythiophene copolymer containing biocompatible/biodegradable side chains for use as an (electro)active surface in biomedical applications, *Polymer Chemistry* 10, 5010-5022 (2019). DOI: https://doi.org/10.1039/C9PY00926D (IF: 5.364)

95. G. Fundueanu, M. Constantin, S. Bucatariu, P. Ascenzi, Poly(N-isopropylacrylamide-co-N-vinylpyrrolidone) thermoresponsive microspheres: The low drug loading ensures the pulsatile release mechanism, *Express Polymer Letters* 14, 63-76 (2019). DOI: https://doi.org/10.3144/expresspolymlett.2020.6 (IF: 3.952)
96. M. Constantin, S. Bucatariu, P. Ascenzi, M. Butnaru, G. Fundueanu, Smart drug delivery system activated by specific biomolecules, *Materials Science & Engineering C - Materials for Biological Applications* 108, 110466 (2019). DOI: https://doi.org/10.1016/j.msec.2019.110466 (IF: 8.457)
97. E. Tarabukina, A. Rozanova, G. Fundueanu, M. Constantin, V. Harabagiu, A. Filippov, Thermo-sensitivity of poly-N-isopropylacrylamide with statistically introduced d,l-allylglycine betainic units, *Journal of Macromolecular Science Part B - Physics* 58, 100-120 (2019). DOI: https://doi.org/10.1080/00222348.2019.1695379 (IF: 1.366)
98. M. Iacob, C. Racles, M. Dascalu, C. Tugui, V. Lozan, M. Cazacu, Nanomaterials developed by processing iron coordination compounds for biomedical application, *Journal of Nanomaterials* 2019, 2592974, 14 pages (2019). DOI https://doi.org/10.1155/2019/2592974 (IF: 3.791)
99. C. Racles, M. Cazacu, M. Zaltariov, M. Iacob, M. Butnaru, Siloxane-based compounds with tailored surface properties for health and environment, *Phosphorus, Sulfur, and Silicon and the Related Elements* 194, 1-6 (2019). DOI: https://doi.org/10.1080/10426507.2019.1630405 (IF: 1.052)
100. G.-O. Turcan-Trofin, M.-F. Zaltariov, G. Roman, S. Shova, N. Vornicu, M. Balan-Porcarasu, D. L. Isac, A. Neamtu, M. Cazacu, Amphiphilic silicone-bridged bis-triazoles as effective, selective metal ligands and biologically active agents in lipophilic environment, *Journal of Molecular Liquids* 294, 111560 (2019). DOI: https://doi.org/10.1016/j.molliq.2019.111560 (IF: 6.633).
101. C. Tugui, V. Tiron, M. Dascalu, L. Sacarescu, M. Cazacu, From ultra-high molecular weight polydimethylsiloxane to super-soft elastomer, *European Polymer Journal* 120, 109243 (2019). DOI: https://doi.org/10.1016/j.eurpolymj.2019.109243 (IF: 5.546).

2018

102. G. Cioca, M. Pinteala, E. S. Bacaita, I. Oprea, I. Crumpei Tanasa, S. R. Volovat, V. S. Dragan, S. Trocaru, C. Anton, Nonlinear behaviors in gene therapy: Theoretical and experimental aspects, *Materiale Plastice* 55, 340-343 (2018). https://www.revmaterialeplastice.ro/pdf/18%20CIOCA%203%2018.pdf (IF: 0.782).
103. C. Ma, A. Laaksonen, C. Liu, X. Lu, X. Ji, The peculiar effect of water on ionic liquids and deep eutectic solvents, *Chemical Society Reviews* 47, 8685-8720 (2018). DOI: https://doi.org/10.1039/C8CS00325D (IF: 60.615)

Book Chapters with acknowledgments at the 5D-nanoP project

2022

1. Carlo Maria Carbonaro, Leon Engelbrecht, Chiara Olla, Antonio Cappai, Maria Francesca Casula, Claudio Melis, Luigi Stagi, Aatto Laaksonen and Francesca Mocci, Graphene Quantum Dots and Carbon Nanodots: modelling of zero-dimensional carbon nanomaterials, in *Zero dimensional carbon nanomaterials: Material design methods, properties and applications*, Editor: J. Kuruvilla, Elsevier Science (2021).

2021

2. L. Engelbrecht, F. Mocci, Y. Wang, S. Perepelytsya, T. Vasiliu, A. Laaksonen, Molecular Perspective on Solutions and Liquid Mixtures from Modelling & Experiment. Chapter 3 in *Soft Matter Systems for Biomedical Applications*, Editors: L. Bulavin, N. Lebovka, Springer Nature Switzerland AG (2021). DOI: https://doi.org/10.1007/978-3-030-80924-9
3. F. Mocci, A. Laaksonen, L. Engelbrecht, T. Vasiliu, S. Perepelytsya, DNA-polyamine interactions: Insight from Molecular Dynamics simulations on the sequence-specific binding of spermidine. Chapter 4 in *Soft Matter Systems for Biomedical Applications*, Editors: L. Bulavin, N. Lebovka, Springer Nature Switzerland AG (2021). DOI: https://doi.org/10.1007/978-3-030-80924-9
4. A. Lyubartsev, A, Laaksonen, Inverse Problems and Hierarchical Multiscale Modelling of Biological Matter. Pages 213-238, in *New Trends in Macromolecular and Supramolecular Chemistry for Biological Applications*, Editors: M.J.M. Abadie, M. Pinteala, A. Rotaru, Springer Nature Switzerland AG (2021). https://doi.org/10.1007/978-3-030-57456-7

2018

5. M. Fossepre, L. Leherte, A. Laaksonen, D. P. Vercauteren, Understanding the Structure and Dynamics of Small Peptides and Proteins Through the Lens of Network Science, in *Biomolecular Simulations in Structure-Based Drug Discovery* (Editors: F. L. Cervasion and V. Spiwok), Wiley-VCH Verlag (2018).

Participation at Conferences / Symposiums with acknowledgments at the 5D-nanoP project

2022

1. A. Laaksonen, *Inverse Problems and Hierarchical Multiscale Modelling of Biological Matter*, Biodynamics – a Transdisciplinary Approach, Bucharest, May 19-21 organized by Romanian Academy & Institute of Biodynamics (**Invited Speaker**)

2. C. Deleanu, Some tips and tricks for NMR metabolomics and lipidomics, Magnetic Moments in Central Europe 2022 (MMCE 2022), 01-04th of June 2022, Primošten, Croatia (**Invited Speaker**)

3. D.M. Suflet, I. Popescu, I.M. Pelin, D. Serbezeanu, A.A. Enache, M. Bercea, *Polysaccharide-based electrospun nanofibers. Preparation and characterization*, Proceedings, International Conference on Rheology "Understanding the Viscoelastic Behavior of Materials – Progress and Challenges", May 26th, 2022, Iasi, Romania, pp. B15-B19 (Online scientific event) (**Proceedings**)

4. G. Fundueanu, B. Cosman, S. Bucatariu, M. Constantin, *Smart microparticulate systems for the transport and controlled delivery of doxorubicin to tumor cells*, 32nd Edition of the International Congress of Apollonia University "Preparing the future by promoting excellence", 28.02-1.03.2022, Iasi, Romania (**Oral Presentation**)

5. B. Cosman, M. Constantin, M. Bercea, G.L. Ailiesei, G. Fundueanu, *pH/thermosensitive copolymer with gelling properties for controlled delivery of drugs*, 32nd Edition of the International Congress of Apollonia University "Preparing the future by promoting excellence", 28.02-1.03.2022, Iasi, Romania (**Oral Presentation**)

6. I.M. Pelin, I. Popescu, D.L. Ichim, M. Constantin, G. Fundueanu, *Synthesis, characterization and biological activity of Pullulan-PVA hydrogels loaded with Calendula officianilis extract*, 32nd Edition of the International Congress of Apollonia University "Preparing the future by promoting excellence", 28.02-1.03.2022, Iasi, Romania (**Oral Presentation**)

7. S. Bucatariu, B. Cosman, M. Constantin, G. Fundueanu, *An interpenetrating polymeric scaffold based on hyaluronic acid and a thermosensitive polymer for biomedical applications*, 32nd Edition of the International Congress of Apollonia University "Preparing the future by promoting excellence", 28.02-1.03.2022, Iasi, Romania (**Oral Presentation**)

8. M. Zaltariov, N. Vornicu, M. Cazacu, C. Tugui, B.I. Ciubotaru, *Silicone materials-from cultural heritage conservation to biomedical applications*, International Scientific Conference "Yesterday's cultural heritage - implications for the development of tomorrow's sustainable society" 5th edition. Scientific event held in the context of the International Day of Women in Science - February 22, 2022, Chisinau – conference (**Oral Presentation**)

9. M.F. Zaltariov, A. Bargan, D. Peptanariu, C. Cojocaru, B.-I. Ciubotaru, M. Cazacu, *Bioactive and biodegradable silatranes as potential functional entities for nanoplatforms of biomedical relevance*, International Congress of the "Apollonia" University of Iasi Preparing the future by promoting excellence, XXXII Edition, February 28 - March 2, 2022, Iasi, Romania – oral communication (**Oral Presentation**)

10. A.-D. Bendrea, L. Cianga, G.-E. Hitruc, I. Popescu, I. Cianga, *Enzyme-activatable nanoplatforms based on PEG-grafted π-conjugated amphiphilic copolymers designed for synergistic cancer diagnosis and dual-mode photodynamic and chemotherapy*, Congresul International "Pregatim viitorul promovand excelenta", Editia a XXXII-a Universitatea "Apollonia" IASI, 28 februarie-2 martie 2022 (**Oral Presentation**)

11. A.-D. Bendrea, L. Cianga, E.Armelin, C. Aleman, I. Cianga, *Conjugated electroactive polymers as advanced materials for tissue engineering: The "hairy-rod" architecture as an emerging alternative*, The 3rd International Congress on Advanced Materials Science and Engineering, AMSE 2022, 21-25 July 2022, Opatija, Croatia; https://www.istci.org/AMSE2022/ (**Oral Presentation**)

12. D.M. Suflet, I. Popescu, I.M. Pelin, D. Serbezeanu, A.A. Enache, M. Bercea, *Polysaccharide-based electrospun nanofibers. Preparation and characterization*, International Conference on Rheology Understanding the Viscoelastic Behavior of Materials – Progress and Challenges, May 26th, 2022, Iasi, Romania (**Poster**)

13. M. Calin, C.A. Mocanu, G. Voicu, F. Safciuc, I. Manduteanu, M. Simionescu, *Endothelium-targeted RAGE-shRNA nanocarriers reduce atherosclerosis-associated inflammation*, 7th International Congress on Biomaterials & Biosensors (BIOMATSEN2022), 22-28 April 2022, Fethiye – Mugla, Turkey (**Poster**)

14. M. Turtoi, M. Anghelache, M. Deleanu, G. Voicu, F. Safciuc, A.A. Patrascu, D-L. Popescu, M. Calin, *Design and antitumor activity of a new vanadium-based compound*, The 19th International Conference on Nanosciences & Nanotechnologies (NN22), 5-8 July 2022, Thessaloniki, Greece (on-line) (**Poster**)

2021

15. B. Cosman, S. Bucatariu, M. Constantin, G. Fundueanu, *pH/Temperature-sensitive interpenetrating polymeric hydrogel*, ICMPP – Open Door to The Future. Scientific Communications of Young Researchers, MacroYouth'2021, 19.11. 2021, Iasi, Romania (**Oral Presentation**)

16. M. Calin, *P-selectin directed RAGE-shRNA nanocarriers reduce atherosclerosis-associated inflammation in ApoE-deficient mice*, The 42nd Anniversary Symposium of the Institute of Cellular Biology and Pathology "Nicolae Simionescu" and the 38th Annual Scientific Session of the Romanian Society for Cell Biology, 4-6 November 2021, online session (**Oral Presentation**)

17. A. Arvinte, *Bimetallic Based Nanostructures for Electrochemical Sensing Applications*, 6th International Congress on Biomaterials and Biosensors (BIOMATSEN), Oludeniz, Turkey, 17-23 October 2021 (**Oral Presentation**)

18. M. Turtoi, *Hyaluronic acid-based 3D cell model of human hepatocarcinoma for chemotherapeutic drug testing*, 5DnanoP Workshop2021 at Petru Poni Institute, 11 October 2021, online session (**Oral Presentation**)

19. P. Tirnovan, F. Mocci, T. Vasiliu, L. Cianga, I. Cianga, M. Pinteala, A. Laaksonen, *In silico studies of a novel amphiphilic graft conjugated polymer for biomedical applications*, 5DnanoP Workshop2021 at Petru Poni Institute, 11 October 2021, online session (**Oral Presentation**)

20. C. Racles, M.-F. Zaltariov, D. Peptanariu, T. Vasiliu, M. Cazacu, *Functionalized silica as doxorubicin carriers*, 5DnanoP Workshop2021 at Petru Poni Institute, 11 October 2021, online session (**Oral Presentation**)

21. M.-F. Zaltariov, M. Cazacu, D. Peptanariu, C. Cojocaru, L. Clima, B.-I. Ciubotaru, A. Bargan, *New silatranes possesing biodegradable and bioactive functionalities*, 5DnanoP Workshop2021 at Petru Poni Institute, 11 October 2021, online session (**Oral Presentation**)

22. A.-D. Bendrea, L. Cianga, I. Cianga, *Regarding some of the potential application uses of the unexpected scientific findings during the research of 5DnanoP*, 5DnanoP Workshop2021 at Petru Poni Institute, 11 October 2021, online session (**Oral Presentation**)

23. I. Cianga, A.-D. Bendrea, L. Cianga, G.-L. Ailiesiei, *Conducting conjugated polymers as biomaterials in the frame of 5DnanoP project*, 5DnanoP Workshop2021 at Petru Poni Institute, 11 October 2021, online session (**Oral Presentation**)

24. A.-D. Bendrea, L. Cianga, I. Cianga, *Thiophene end-group functionalized oligo(2-methyl-2-oxazoline) as an amphilphilic reactive macromonomer and as a non-conventional intrinsic luminescent material*, Conference "Progress in Organic and Macromoleculecular Compounds", 7-9 October 2021, Iasi, Romania (**Oral Presentation**)

25. B.F. Craciun, L. Clima, A. Angeli, A. Petreni, S.A. Ibanescu, M. Pinteala, C.T. Supuran, *Squalene functionalized with coumarines or benzenesulfonamides as hybrid inhibitors for Carbonic Anhydrase*, Progress in Organic and Macromolecular Compounds 28th edition "MACROIasi 2021", Iasi, Romania, October 7-9 2021 (**Poster Presentation**)

26. A. Laaksonen, *Multiscale modelling of ionic liquids and biomass*. Young Scientists Workshop on Conversion and Utilization of Biomass, September 28-29, 2021, Beijing China (**Plenary Speaker**)

27. C. Deleanu, *NMR metabolomics and lipidomics in clinical diagnosis*, Adriatic NMR Conference, 13-15.09.2021, Primosten, Croatia. Book of Abstracts, pp. 19, ISSN 2806-6227 (**Plenary Speaker**)

28. G. Fundueanu, *Stimuli-sensitive polymers for self-regulated drug delivery systems*, United Conference of Pharma B2B, Novel Trends and Approaches in Pharmaceutical Industry, July 15, 2021, New Jersey, USA (**Keynote Conference**)

29. I. Popescu, M. Turtoi, R.N. Darie-Nita, M. Calin, *Degradable Pluronic/alginate hydrogels for skin wound healing-in vitro studies*, International Congress of the „Apollonia" University from Iasi „By promoting excellence, we prepare the future" XXXIth Edition, 01-03.03. 2021, Iasi, Romania (**Oral Presentation**)

30. A.-D. Bendrea, L. Cianga, I. Cianga, *Conjugated polymers: a step forward to smarter and more advanced synthetic polymers biomaterials*, The International Congress of Apolonia University of Iasi, 1-3 March 2021, Iasi, Romania (**Oral Presentation**)

31. M. Turtoi, M. Anghelach, D.-L. Popescu, I. Manduteanu, M. Calin, *Design of new oxidovanadium(V) compounds as insulin-mimetics*, The 42nd Anniversary Symposium of the Institute of Cellular Biology and

Pathology "Nicolae Simionescu" and the 38th Annual Scientific Session of the Romanian Society for Cell Biology, 4-6 November 2021, online session (**Poster**)

32. G. Voicu, M. Turtoi, M. Anghelache, S.-M. Bucatariu, M. Deleanu, F. Safciuc, I. Manduteanu, Ghe. Fundueanu, M. Simionescu, M. Calin, *A three-dimensional hyaluronic acid-based scaffold seeded with human cancer cells functions as a suitable platform for antitumoral drug screening*, The 18th International Conference on Nanosciences & Nanotechnologies (NN21), 6-9 July 2021, Thessaloniki, Greece (**Poster**)

33. M. Turtoi, M. Anghelache, A.-A. Patrascu, C. Maxim, D.-L. Popescu, I. Manduteanu, M. Calin, *Designing of new biocompatible coordinating compounds of oxidovanadium(V) as insulin mimetics*, The 18th International Conference on Nanosciences & Nanotechnologies (NN21), 6-9 July 2021, Thessaloniki, Greece (**Poster**)

34. F. Zaltariov, C.D. Varganici, D. Filip, D. Macocinschi, *Stability of the HPC/PU Polymeric Blends in Accelerated Weathering and Biological Environments*, 1st Corrosion and Materials Degradation Web Conference, 17-19 May 2021, sciforum ID-045074 (**Poster**)

2020

35. G. Fundueanu, M. Constantin, *Polymeric micro- and nano-particles for drug delivery*, International Congress of „Apollonia" University from Iasi, By promoting excellence, we prepare the future, Edition XXX, Iasi, Romania, 27th of February – 1st of March, 2020 (**Invited Speaker**)

36. S. Bucatariu, M. Constantin, G. Fundueanu, M. Calin, *A new sponge-type hydrogel as a 3D support for tumoral cell culture*, The 5th International Conference on Chemical Engineering (ICCE 2020), Iasi, Romania, 28-30th of October, 2020 (**Oral Presentation**)

37. I. Popescu, M. Constantin, *Stimuli-sensitive pluronic-alginate hydrogels formed by photoinitiated thiol-ene reaction*, International Congress of „Apollonia" University from Iasi, By promoting excellence, we prepare the future, Edition XXX, Iasi, Romania, 27th of February – 1st of March, 2020 (**Oral Presentation**)

38. I. M. Pelin, D. M. Suflet, I. Popescu, *Hydrogel as component for buccal patches: synthesis, characterization and antibiotic release*, International Congress of „Apollonia" University from Iasi, By promoting excellence, we prepare the future, Edition XXX, Iasi, Romania, 27th of February – 1st of March, 2020 (**Oral Presentation**)

39. D. L. Isac, A. Coroaba, T. Vasiliu, R. Zonda, S.-A. Ibanescu, C. Al Matarneh, A. Airinei, M. Pinteala, *Interplay of electronic structure in ground and excited states of new di-iminopyrene-di-benzo-18-crown-6-ether derivative by TD-DFT studies*, The 5th International Conference on Chemical Engineering (ICCE 2020), Iasi, Romania, October 28-30th, 2020 (**Oral Presentation**)

40. B.-I. Ciubotaru, M.-F. Zaltariov, M. Cazacu, C. Racles, *Functionalized mesoporous silica in drug delivery and biomedical applications*, International Congress of „Apollonia" University from Iasi, By promoting excellence, we prepare the future, Edition XXX, Iasi, Romania, 27th of February – 1st of March, 2020 (**Oral Presentation**)

41. B.-I. Ciubotaru, M. Cazacu, *Evaluation of silicone-based biomaterials from the bio-and mucoadhesive perspective*, Scientific communications session of young researchers, PPIMC - Open door to the future (MacroYouth'2020), 1st Edition, Iasi, Romania, November 19th, 2020 (**Oral Presentation**)

42. A.-D. Bendrea, L. Cianga, G.-L. Ailiesei, I. Cianga, *Fluorescent EDOT-functionalized poly-ε-caprolactone: Synthesis, photophysical and self-assembling properties in organic solvents and its serendipitously noticed behaviour in protonated media* (on-line registration doi:10.3390/CGPM2020-07208), The First International Conference on „Green" Polymer Materials, November 05-25th, 2020 – online (**Oral Presentation**)

43. A.-D. Bendrea, L. Cianga, I. Cianga, *Graft Conjugated Polymers: Toward Smarter and Versatile Materials for Biomedical Applications*, The 5th International Conference on Chemical Engineering (ICCE 2020), Iasi, Romania, October 28-30th, 2020, (**Poster communication**)

44. S. Bucatariu, G. Fundueanu, M. Constantin, *Design of hyaluronan scaffold via solvent free thermal cross-linking method*, International Congress of „Apollonia" University from Iasi, By promoting excellence, we prepare the future, Edition XXX, Iasi, Romania, 27th of February – 1st of March, 2020 (**Poster**)

2019

45. B.-I. Ciubotaru, M.-F. Zaltariov, C. Racles, M. Cazacu, *Preparation and application of mesoporous silica for pH-controlled delivery of doxorubicin*, Zilele Universităţii „Alexandru Ioan Cuza" din Iasi, Conferinta Facultaţii de Chimie (IasiChem 2019), Iasi, Romania, 31 Octombrie - 01 noiembrie, 2019 (**Poster**)

46. B.-I. Ciubotaru, M.-F. Zaltariov, C. Racles, M. Cazacu, *Functionalized mesoporous silica as carrier for controlled delivery of doxorubicin*, "Zilele Spitalului Clinic C.F. Iasi" 2019 – Performanta Stiintei – Stiinta Performantei, Iasi, Romania, 22-27 octombrie 2019 (**Poster**)
47. M. Calin, *Nanoplatforms for targeted delivery of drugs to activated endothelium*, 9th Annual World Congress of Nano Science & Technology-2019 (Nano S&T-2019), Suzhou, China, October 20-22, 2019 (**Invited Speaker**)
48. M. Carnuta, M. Anghelache, A. A. Patrascu, C. Maxim, D.-L. Popescu, M. Calin, *Synthesis, characterization and in vitro antitumor evaluation of new binuclear oxovanadium(V) compounds*, Achievements and Perspectives of Modern Chemistry, Chisinau, Republica Moldova, October 9-11, 2019 (**Poster**)
49. A.-D. Bendrea, L. Cianga, I. Cianga, *The simplest is the most sophisticated: A Janus type polythiophene copolymer at work for a biointegrable device*, 27th edition of scientific communications entitled "Progress in the field of macromolecular and organic compounds" organized in the frame of Academic Days of Iasi, Iasi, Romania, 2-4 October 2019 (**Oral Presentation**)
50. M. Carnuta, A. A. Patrascu, C. Maxim, M. Anghelache, I. Manduteanu, D.-L. Popescu, M. Calin, *A new family of vanadium compounds stimulates insulin receptor phosphorylation in HepG2 cells in a time and dose-dependent manner*, Anniversary Symposium "An incredible 40-year journey to uncover cell's secrets for the benefit of human health", workshop "Cardiac valves disease: new targets for therapies and tissue engineering", Bucuresti, România, September 19-20, 2019 (**Poster**)
51. S. Bucatariu, M. Constantin, G. Fundueanu, *Design and development of sponge-type hydrogel composed of hyaluronic acid and poly(methylvinylether-alt-maleic acid) for biomedical applications*, 21st Romanian International Conference on Chemistry and Chemical Engineering (RICCCE 2019), Constanta, Romania, September 4-7, 2019 (**Oral Presentation**)
52. I. Popescu, M. Constantin, *Alginate-pluronic hydrogels obtained by thiol-ene photo-click reaction*, 21st Romanian International Conference on Chemistry and Chemical Engineering (RICCCE 2019), Constanta, Romania, September 4-7, 2019 (**Oral Presentation**)
53. I.M. Pelin, I. Popescu, D.M. Suflet, *Phosphorylated curdlan based hydrogels for medical applications*, 21st Romanian International Conference on Chemistry and Chemical Engineering (RICCCE 2019), Constanta, Romania, September 4-7, 2019 (**Oral Presentation**)
54. M. Carnuta, A. A. Patrascu, C. Maxim, M. Anghelache, M. Calin, D.-L. Popescu, *Synthesis and characterization of a new vanadium (V) complex based on D/L-valine Schiff base with anti-cancer properties*, 21st Romanian International Conference on Chemistry and Chemical Engineering (RICCCE 2019), Constanta, Romania, September 4-7, 2019 (**Poster**)
55. M. Carnuta, A. A. Patrascu, C. Maxim, M. Anghelache, I. Manduteanu, D.-L. Popescu, M. Calin, *A new family of vanadium compounds stimulates insulin receptor phosphorylation in HepG2 cells in a time and dose-dependent manner*, The 37th Annual Scientific Session of the Romanian Society for Cell Biology and the 11th National Congress with International Participation", Constanța, Romania, June 20-23, 2019 (**Poster**)
56. G. David, M. Iachim, G. Pricop, A. Bargan, I. Rosca, *Hybrid 3D polymer matrices- evaluation for biomedical applications*, Al 13-lea simpozion international de produse cosmetice si aromatizante, Cosmetologia – esenta de frumos si sanatate, Iasi, Romania, 4-7 iunie, 2019 (**Oral Presentation**)
57. G. Fundueanu, M. Constantin, S. Bucatariu, *Advanced polymeric materials in drug delivery*, 29th edition of International Congress of "Apollonia" University from Iasi, Iasi, Romania, 28 February - 3 March 2019 (**Oral Presentation**)
58. D.M. Suflet, *Ionic curdlan hydrogels for medical and pharmaceutical application*, 29th edition of International Congress of "Apollonia" University from Iasi, Iasi, Romania, 28 February - 3 March 2019 (**Oral Presentation**)

2018

59. C. Racles, M. Cazacu, M. Zaltariov, M. Iacob, M. Butnaru, *Siloxane-based compounds with tailored surface properties for health and environment*, International Conference On Phosphorus, Boron And Silicon, PBSi 2018, Barcelona, Spain, December 10-12, 2018 (**Oral Presentation**)
60. M. Pinteala, *Nanoparticles in Theragnostics Approach: Synthesis, Structure, Particularities*, Nuclear Medicine Days, Iasi, Romania, November 1-4, 2018 (**Invited Conference Presentation**)
61. S. Bucatariu, M. Constantin, G. Fundueanu, *pH/temperature-sensitive microgels for self-regulated drug delivery systems*, 4th International Conference on Chemical Engineering, Iasi, Romania, 31 October - 02 November 2018 (**Oral Presentation**)

62. L.G. Ailiesei, L. Cianga, A.D. Bendrea, E.G. Hitruc, I. Cianga, *What link can NMR Spectroscopy have with AFM Microscopy? – Unraveling complex configurational and supramolecular organization in conjugated polymers*, Chemistry Faculty Conference (Chem 2018), Iasi, Romania, October 25-26, 2018 (**Oral communication**)

Training Sessions / Invited Trainers / Internships

2022

1. Dr. Natalia Simionescu, Institute of Cellular Biology and Pathology "Nicolae Simionescu", Bucharest Romania (2 weeks), **Short research stay**

2019

2. Dr. Anca Dana Bendrea, "Grigore T. Popa" University of Medicine and Pharmacy of Iasi, Faculty of Biomedical Engineering, Centre for Tissue Engineering and Regenerative Medicine, Iasi, Romania, 30 May-20 June 2019, **Short-period training** course entitled "***In vitro* and *in vivo* testing methods for regenerative medicine**".

2018

3. Prof. Francesca Mocci, University of Cagliari, Italy in "Petru Poni" Institute of Macromolecular Chemistry, September 4- 25, 2018; **Invited Trainer**.
4. Prof. Francesca Mocci, University of Cagliari, Italy in "Petru Poni" Institute of Macromolecular Chemistry, 31 October- 4 December 2018; **Invited Trainer**.
5. Dr. Narcisa Marangoci, Institute of Polymer Research Dresden, Germany, November 22-30, 2018; **Short Stay**.
6. Dr. Anca Bendrea, Universitat Politecnica de Catalunia, Departament d'Enginerya Quimica and Barcelona Research Center for Multiscale Science and Engineering (Prof. Carlos Aleman, Prof. Elaine Armelin, Barcelona, 30 October-9 November 2018; **Training Session**.
7. Dr. Mariana Pinteala, University of Firenze, Italy, 4 September-12 September 2018; **Short Stay**.
8. Dr. Stelian Maier, University of Firenze, Italy, 4 September-12 September 2018; **Short Stay**.
9. Acad. Bogdan C. Simionescu, University of Firenze, Italy, 4 September-12 September 2018; **Short Stay**.

Meetings between partners

2022

1. January 27, 2022, 12-16 h, Petru Poni Institute, Iasi, Romania (online)
2. March 18, 2022, 10-16 h, Petru Poni Institute, Iasi, Romania (online)

Workshops

2022

1. 5D-nanoP Workshop, June 15, 2022, 10-18 h, Petru Poni Institute, Iasi, Romania (online).
Andrei Neamtu "Unorthodox hybrid MD simulations of ion channels"
Tudor Vasiliu "On the minor groove binders"
Dragos Isac "Simulating a heterografted polythiophene copolymer. A comparison between implicit and explicit solvent models"

2021

2. 5DnanoP Workshop2021 at Petru Poni Institute, October 11th, 2021, Iasi, Romania.

2018

3. Dr. Mariana Pinteala, IMAGO-MOL Cluster Meeting: 2nd Meeting of the Working Group on the Establishment of the National Center for Nuclear Medicine. **Presentation, and signing of the Nuclear Medicine Consortium Memorandum**, November 03, 2018, Iasi, Romania.
4. Dr. Adina Coroaba, IMAGO-MOL Cluster Meeting: 2nd Meeting of the Working Group on the Establishment of the National Center for Nuclear Medicine, November 03, 2018, Iasi, Romania.

PhD thesis with acknowledgments at the 5D-nanoP project

2021

1. *New polymer networks based on modified polysaccharides, with potential medical applications*, PhD Student – Ioana A. Tanasa (Duceac), Scientific Supervisor – Dr. Sergiu Coseri

2020

2. *Conjugates for genes and drugs delivery*, PhD Student – Bogdan Florin Craciun, Scientific Supervisor – Dr. Mariana Pinteala.
3. *Self-assembled dynamic macromolecular systems: Molecular modeling and experimental validation studies*, PhD Student – Tudor Vasiliu, Scientific Supervisor – Dr. Mariana Pinteala.

Project Website

https://www.intelcentru.ro/5D-nanoP/ro/
https://www.intelcentru.ro/5D-nanoP/

Project Director,

Prof. Aatto Laaksonen, PhD