NORTE2020
PROGRAMA OPERACIONAL REGIONAL DO NORTE

Project

SUSTAINABLE ADVANCED MATERIALS (SAM)

Project code: NORTE-01-0145-FEDER-000028

Coordinator: António Fernando Sousa da Silva

Report nº2

For the period: 01/06/2016 to 31/05/2019

Introduction

The objectives of this project were to investigate relevant physical and chemical properties of novel and existing organic materials and their practical applications to sustainable technologies related to renewable energies and to different areas of industry such as electronics, food, pharmaceutical, cosmetic, and health sciences. The environmental impact of some of these compounds was also evaluated using predictive equations developed during this project.

Accordingly the research objectives were structured in four research tasks:

1. BIOANTIOX -Bio-based Products for Fighting Oxidative Processes
2. NANODEL - Smart Nanosystems for Controlled Delivery
3. FUNCOAT -Functional Nanocoatings
4. MENERG -Materials for Energy Production, Storage and Transport

aiming at the development of:

i) Biobased antioxidants to be used either as additives or for health application in the prevention and/or therapy of oxidative stress-related diseases;

ii) Different nano-structured systems for the loading, transport and smart delivery of biomolecules;

iii) Functional nanocoatings aimed at modifying the surface of materials resulting in highly advanced materials with specific functions;

iv) Highly efficient energy production, involving semiconductors synthesized by organic matter and bio-fuels, as well as developing transport and storage materials and devices.

The present report accounts for the activities and results obtained in each individual task

Summary of results

The work plan has been carried out according to the approved proposal, without deviations.

The total number of scientific publications was:

Edited Books: 1

Book Chapters: 7

Scientific Papers: 140

PhD theses: 26

Concluded: 14

In progress: 12

Master theses: 10

Patents: 4

Technology Transfer: 2

2.1 Tarefa BIOANTIOX - Bio-based Products for Fighting Oxidative Processes

Investigador responsável: Profª Doutora Fernanda Borges

Goals:
i) Development of bio-based antioxidants;
ii) Evaluation of the antioxidant capacity and physicochemical properties of the bio-based antioxidant systems;
iii) Evaluation of the health benefits, safety and bioavailability properties of the biobased antioxidant systems;
iv) Evaluation of the effect of biobased antioxidants on oxidation stability of diverse industry matrices;
v) Development of nanoengineered biobased antioxidants.

2.1.1. Description of activities and results

- Novel, potent and safe biobased antioxidants have been obtained by biology-oriented synthesis (BIOS) using natural synthons and sustainable biomimetic approaches (see publications 7, 8, 12, 14, 16, 19, 20, 24, 26-28, 33).

- The antioxidant and physicochemical properties of developed bio-based antioxidants have been obtained. The data allow to establish structure-(property)-activity relationships and provide key information to obtain the guidelines for the chemical optimization of systems (see publications 7, 8, 12, 15, 24, 26-28, 32, 33).

- The evaluation of biological, safety and bioavailability properties of the obtained bio-based antioxidants have been performed. Relevant performance toward health-promoting events was attained for several systems (see publications 5,7, 8, 12, 16, 18, 19, 20, 24-31, 33).

- New nanoengineered antioxidants were developed to circumvent constrains arising from poor stability, solubility and/or bioavailability of natural based systems. Innovative delivery systems able to improve their bioactivity and broaden their application in the therapy towards age-related disorders have been developed (see publications 21, 22, 23).

- The state of the art of the systems and their applications have been reviewed (see publications 1- 4, 6, 9, 13, 17, 34).

- Novel bioinformatic tools have been developed (see publications 3, 10, 11).

2.1.2. Deviations from the approved project

No deviations are reported.

2.1.3. Scientific Publications

Book chapters

1. Fernandes, C; Benfeito, S.; Fonseca, A.; Oliveira, C.; Garrido, J.; Garrido, E. M.; Borges, F. Photodamage and photoprotection: towards safety and sustainability through nanotechnology solutions. In *FoodPreservation, in Nanotechnology in the Agri-Food Industry series (Muti-Volume SET I-X)*; Grumezescu, A., Ed.; Academic Press, Elsevier, **2017**; pp. 527-565. eBook ISBN: 9780128043745, Hardcover ISBN: 9780128043035.

2. Amorim, R.; Benfeito, S.; Teixeira, J.; Cagide, F.; Oliveira, P. J.; Borges, F. Targeting mitochondria: the road to mitochondriotropic antioxidants and beyond. In *Mitochondrial*

Biology and Experimental Therapeutics; Oliveira, P. J., Ed.; Springer, **2018**; pp. 333-358. eBook ISBN: 9783319733449, Hardcover ISBN: 9783319733432.

3. Perez-Castillo, Y., Sotomayor-Burneo, S., Helguera, A. M., Cordeiro, M. N. D. S., Tejera, E., Pazy-Miño, C., Sánchez-Rodríguez, A., Moreno, M. F., Teijeira-Bautista, M., Ancede-Gallardo, E., Borges, F., & Cruz-Monteagudo, M. Computer-aided Drug Discovery Methodologies in the Modeling of Dual Target Ligands as Potential Parkinson's Disease Therapeutics. In: *Frontiers in Computational Chemistry*, Zaheer-ul-Haq Qasmi, Z. H., & Madura, J.D. Eds, Bentham Sciences Publisher **2018** Vol. 4, pp. 3-52. ISBN (Online): 978-1-68108-441-1. ISBN (Print): 978-1-68108-442-8.

4. Pinto, M.; Benfeito, S.; Fernandes, C.; Borges, F. Blood-brain barrier, oxidative stress and dietary antioxidants. In *Oxidative Stress and Dietary Antioxidants in Neurological Diseases*; Preedy, V. R. and Martins, C., Eds.; Academic Press, Elsevier, **2019** (in press).

Articles

1. Silva, T.; Mohamed, T.; Shakeri, A.; Rao, P.; Martínez-González, L.; Pérez, D.; Martínez, A.; Valente, M. J.; Garrido, J.; Uriarte, E.; Serrão, P.; Soares-da-Silva, P.; Remião, F.; Borges, F. Development of Blood–Brain Barrier Permeable Nitrocatechol-Based Catechol O-Methyltransferase Inhibitors with Reduced Potential for Hepatotoxicity. *J. Med. Chem.* **2016**, *59(16)*, pp. 7584–7597.

2. Chavarria, D.; Silva, T.; Magalhães, D.; Remião, F.; Borges, F. Lessons from black pepper: piperine and derivatives thereof. *Expert Opin. Ther. Pat.* **2016**, *26(2)*, pp. 245-64.

3. Teixeira, J.; Cagide, F.; Benfeito, S.; Soares, P.; Garrido, J.; Baldeiras, I.; Ribeiro, J.; Pereira, C.; Silva, A. F.; Andrade, P.; Oliveira, P. J.; Borges, F. Development of a mitochondriotropic antioxidant based on caffeic acid: proof of concept on cellular and mitochondrial oxidative stress model. *J. Med. Chem.* **2017**, *60(16)*, pp. 7084-7098.

4. Teixeira, J.; Oliveira, C.; Amorim, R.; Cagide, F.; Garrido, J.; Ribeiro, J.; Pereira, C. M.; Silva, A. F.; Andrade, P. B.; Oliveira, P. J.; Borges F. Development of hydroxybenzoic-based platforms as a solution to deliver dietary antioxidants to mitochondria. *Sci. Rep.* **2017**, *7(1)*, pp. 6842.

5. Teixeira J.; Chavarria, D.; Borges, F.; Wojtczak, L.; Wieckowsk, M. R.; Karkucińska-Wieckowska, A.; Oliveira, P. J. Dietary Polyphenols and Mitochondrial Function: Role in Health and Disease. *Curr. Med. Chem.* **2017**, *24(42)*, pp.1-27.

6. Cruz-Monteagudo, M.; Schürer, S.; Tejera, E.; Perez-Castillo, Y.; Medina-Franco, J. L.; Sanchez-Rodriguez, A.; Borges, F. Systemic QSAR and phenotypic virtual screening: chasing butterflies in drug discovery. *Drug Discov. Today* **2017**, *22(7)*, pp. 994-1007.

7. Sánchez-Rodríguez, A.; Perez-Castillo, Y.; Schürer, S. C.; Nicolotti, O.; Mangiatordi, G. F.; Borges, F.; Cordeiro, N.; Tejera, E.; Medina-Franco, J. L.; Cruz-Monteagudo, M. From flamingo dance to (desirable) drug discovery: a nature-inspired approach. *Drug Discov. Today* **2017**, *22(10)*, pp. 1489-1502.

8. Moosavi, F.; Hosseini, R.; Rajaian, H.; Silva, T; Magalhães, D.; Saso, L.; Edraki, N.; Miri, R.; Borges, F.; Firuzi, O. Derivatives of caffeic acid, a natural antioxidant, as the basis for the discovery of novel nonpeptidic neurotrophic agents. *Bioorg. Med. Chem.* **2017**, *25(12)*, pp. 3235-3246.

9. Oliveira, C.; Benfeito, S.; Fernandes, C.; Cagide, F.; Silva, T.; Borges, F. NO- and HNO-releasing agents, spin traps and nitroxides: past, present and future. *Med. Res. Rev.* **2018**, *38(4)*, pp. 1159-1187.

10. Oliveira, C.; Gaspar, A.; Gomes, L. R.; Low, J. N.; Borges, F.; Cagide, F. Structural elucidation of a series of benzamide derivatives. *Magn. Reson. Chem.* **2018**, *56(3)*, pp. 216-223.

11. Teixeira, J.; Oliveira, C.; Cagide, F.; Amorim, R.; Garrido, J.; Borges, F.; Oliveira, P. J. Discovery of a new mitochondria permeability transition pore (mPTP) inhibitor based on gallic acid. *J. Enzyme Inhib. Med. Chem*. **2018**, *33(1)*, pp. 567-576.

12. Teixeira, J.; Deus, C. M.; Borges, F.; Oliveira, P. J. Targeting mitochondrial reactive oxygen species with mitochondriotropic polyphenolic-based antioxidants. *Int. J. Biochem. Cell Biol.* **2018**, *97*, pp. 98-103.

13. Teixeira, J.; Basit, F.; Swarts, H. G.; Forkink, M.; Oliveira, P. J.; Willems, P. H. G. M; Koopman, W. J. H. Extracellular acidification induces ROS- and mPTP-mediated death in HEK293 cells. *Redox Biol*. **2018**, *15*, pp. 394-404.

14. Teixeira, J.; Amorim, R.; Santos, K.; Soares, P.; Datta, S.; Cortopassi, G. A.; Serafim, T. L.; Sardão, V. A.; Garrido, J.; Borges, F.; Oliveira, P. J. Disruption of mitochondrial function as mechanism for anti-cancer activity of a novel mitochondriotropic menadione derivative. *Toxicology* **2018**, *393*, pp. 123-139.

15. Oliveira, C.; Cagide, F.; Teixeira, J.; Amorim, R.; Sequeira, L.; Mesiti, F.; Silva, T.; Garrido, J.; Remião, F.; Vilar, S.; Uriarte, E.; Oliveira, P. J.; Borges, F. Hydroxybenzoic acid derivatives as dual-target ligands: mitochondriotropic antioxidants and cholinesterase inhibitors. *Front. Chem.* **2018**, *6*, pp.1-17.

16. Garrido, E. M.; Cerqueira, A.; Chavarria, A.; Silva, T.; Borges, F.; Garrido, J. Microencapsulation of caffeic acid phenethyl ester and caffeic acid phenethyl amide by inclusion in hydroxypropyl-β-cyclodextrin. *Food Chem.* **2018**, *254*, pp. 260-265.

17. Fernandes, C.; Pinto, M.; Martins, C.; Gomes, M. J.; Sarmento, B.; Oliveira, P. J.; Remião, F; Borges, F. Development of a PEGylated-based Platform for Efficient Delivery of Dietary Antioxidants Across the Blood–Brain Barrier. *Bioconj. Chem.* **2018**, *29*, pp. 1677-1689.

18. Fernandes, C.; Benfeito, S.; Amorim, R.; Teixeira, J.; Oliveira, P. J.; Remião, F.; Borges, F. Desrisking the Cytotoxicity of a Mitochondriotropic Antioxidant Based on Caffeic Acid by a PEGylated Strategy. *Bioconj. Chem.* **2018**, *29(8)*, pp. 2723-2733.

19. Reis, J; Cagide, F.; Valencia, M. E.; Teixeira J.; Bagetta, D.; Pérez, C.; Uriarte, E.; Oliveira P. J.; Ortuso, F.; Alcaro, S.; Rodríguez-Franco, M. I.; Borges, F. Multi-target-directed ligands for

Alzheimer's disease: Discovery of chromone-based monoamine oxidase/cholinesterase inhibitors. *Eur. J. Med. Chem.* **2018**, *158(5)*, pp. 781-800.

20. Reis, J.; Manzella, N; Cagide, F.; Mialet-Perez, J.; Uriarte, E.; Parini, A.; Borges, F.; Binda, C. Tight-Binding Inhibition of Human Monoamine Oxidase B by Chromone Analogs: A Kinetic, Crystallographic, and Biological Analysis. *J. Med. Chem.* **2018**, *61(9)*, pp. 4203-4212.
21. Hosseini R, Moosavi F, Silva T, Rajaian H, Hosseini SY, Bina S, Saso L, Miri R, Borges F, Firuzi O. Modulation of ERK1/2 and Akt Pathways Involved in the Neurotrophic Action of Caffeic Acid Alkyl Esters. *Molecules.* **2018**, *23*, pp 3340-3346.
22. Oliveira, C.; Bagetta, D.; Cagide, F.; Teixeira, J.; Amorim, R.; Silva, T.; Garrido, J.; Remião, F.; Uriarte, E.; Oliveira, P. J.; Alcaro, S.; Ortuso, F.; Borges, F. Benzoic acid-derived nitrones: A new class of potential acetylcholinesterase inhibitors and neuroprotective agents. *Eur. J. Med. Chem.* **2019**, *174*, pp. 116-129.
23. Benfeito, S.; Oliveira, C.; Fernandes, C.; Cagide, F.; Teixeira, J.; Amorim, R.; Garrido, J.; Martins, C.; Sarmento, B.; Silva, R.; Remião, F.; Uriarte, E.; Oliveira, P. J.; Borges, F. Fine-tuning the neuroprotective and blood-brain barrier permeability profile of multi-target agents designed to prevent progressive mitochondrial dysfunction. *Eur. J. Med. Chem.* **2019**, *167*, pp. 525-545.
24. Gaspar, A.; Mohabbat, M.; Cagide, F.; Razzaghi-Asl, N.; Miri, R.; Firuzi, O.; Borges, F. Searching for new cytotoxic agents based on chromen-4-one and chromane-2,4-dione scaffolds. *Res. Pharm. Sci.* **2019**, *14(1)*, pp. 74-83.
25. Pinheiro S, Serrão MP, Silva T, Borges F, Soares-da-Silva P. Pharmacodynamic evaluation of novel Catechol-O-methyltransferase inhibitors. *Eur J Pharmacol*. **2019** ;*847*, pp. 53-60.
26. Silva, T.; Mohamed, T.; Shakeri, A.; Rao, P. P. N.; Soares da Silva, P.; Remião, F.; Borges, F. Repurposing nitrocatechols: 5-Nitro-α-cyanocarboxamide derivatives of caffeic acid and caffeic acid phenethyl ester effectively inhibit aggregation of tau-derived hexapeptide AcPHF6. *Eur. J. Med. Chem.* **2019**, *167*, pp. 146-152.
27. Pacheco, J. G.; Rebelo, P.; Cagide, F.; Gonçalves, L. M.; Borges, F.; Rodrigues, J. A.; Delerue-Matos, C. Electrochemical sensing of the thyroid hormone thyronamine (T0AM) via molecular imprinted polymers (MIPs). *Talanta* **2019**, *194*, pp. 689-696.
28. Chavarria, C.; Cagide, F.; Pinto, M.; Gomes, L. R.; Low, J. N.; Borges, F. Development of piperic acid-based monoamine oxidase inhibitors: Synthesis, structural characterization and biological evaluation. *J. Mol. Struct.* **2019**, *1182*, pp. 298-307.
29. Mesiti, F.; Chavarria, D.; Gaspar, A.; Alcaro, S.; Borges, F. The chemistry toolbox of multitarget-directed ligands for Alzheimer's disease, *Eur J. Med. Chem.* 2019, accepted for publication.

2.1.4. PhD Thesis

Concluded

1. Ester Sofia Teixeira Benfeito, Design and development of multi-target agents for neurodegenerative diseases

   PhD Thesis, University of Porto, Porto, Portugal, 2018. Supervisor: F. Borges, co-supervisor: F. Remião.

2. Carlos Eduardo Vinhas Fernandes, Development of PEGylated platforms to overcome blood-brain barrier constraints in neurodegenerative therapy

   PhD Thesis, University of Porto, Porto, Portugal, 2018. Supervisor: F. Borges, co-supervisor: F. Remião.

3. Joana Alexandra Costa Reis, Single and multi-target agents for neurodegenerative diseases based on the chromone scaffold

   PhD Thesis, University of Porto, Porto, Portugal, 2018. Supervisor: F. Borges, co-supervisor: E. Uriarte.

4. Ana Catarina Gomes Oliveira, Benzoic acid as a valid scaffold for the development of dual-target directed drugs for Alzheimer's disease

   Ph.D. Thesis University of Porto, Porto, Portugal, 2017, Supervisor: J. Garrido, co-supervisor: F. Borges.

5. André Manuel Ferreira Fonseca, Discovery of target directed drugs for neurodegenerative diseases based on benzopyrone scaffold

   Ph.D. Thesis University of Porto, Porto, Portugal, 2017, Supervisor: F. Borges, co-supervisor: E. Uriarte.

6. Nuno Tiago Barros Silva, Hidroxycinnamic Acid, a Valid Scaffold for the Development of CNS Multitarget Drugs. Synthesis, Pharmacological and Toxicological Studies

   PhD Thesis, University of Porto, Porto, Portugal, 2016. Supervisor: F. Borges, co-supervisors: F. Remião, E. Uriarte.

7. José Carlos Santos Teixeira, Targeting dietary antioxidants to mitochondria: regulating mitochondrial radical production and redox signaling to improve human health

   PhD Thesis, University of Porto, Porto, Portugal, 2016. Supervisor: F. Borges, co-supervisors: P. Andrade.

In progress

1. Daniel Freitas Chavarria, Development of new chemical entities based on natural models with therapeutic potential towards age-related disorders

PhD Thesis, University of Porto, Porto, Portugal.
Supervisor: F. Borges, co-supervisors: P. Oliveira and F. Remião.

2. Ricardo Fernando Santos Amorim, MitoBULLET: Antioxidant Targeting Mitochondria to Prevent Non-Alcoholic Fatty Liver Disease-induced Oxidative Stress and Inflammation
PhD Thesis, University of Coimbra, Coimbra, Portugal.
Supervisor: P. Oliveira, co-supervisors: F. Borges and J. Teixeira.

2.1.5. Master Thesis

Concluded

1. Miguel Rocha Vaz Pinto, Development of effective PEGylated PCL-based nanoformulations for the delivery of potent MAO-B chromone–based inhibitors
Master Thesis, University of Porto, Porto, Portugal, 2017.
Supervisor: F. Borges.

2. Rodrigo Barreto Carreira, Evaluation of antioxidant effects of mitochondria-targeted polyphenolic agents in human skin fibroblasts
Master Thesis, University of Coimbra, Coimbra Portugal, 2018.
Supervisor: J. Teixeira

3. André Filipe dos Santos Barbosa, Targeting dietary antioxidants to mitochondria to modulate redox signaling and metabolism of human fibroblasts
Master Thesis, University of Coimbra, Coimbra, Portugal, 2019.
Supervisor: J. Teixeira.

2.1.6. Patents

Two patents coming out from the results attained along the task BIOANTIOX - Bio-based Products for Fighting Oxidative Processes project have been granted.

- **Title: Hydroxycinnamic derivatives, methods and uses thereof**

Publication number: WO2018069904 (A1); International Application: PCT/IB2017/056412
Publication date: 19.04.2018
Authors: Maria Fernanda Martins Borges, Paulo Jorge Gouveia Simões da Silva Oliveira, José Carlos Santos Teixeira, Fernando Cagide Fagin, Ester Sofia Teixeira Benfeito
Entity: Universidade do Porto & Centro de Neurociências e Biologia Celular

Abstract

The present disclosure relates to the design and development of new hydroxycinnamic derivatives that operate as mitochondriotropic antioxidants. Furthermore, this disclosure is also related to the methods and uses of the hydroxycinnamic derivatives, for example, in the field of human and animal diseases, for instance to treat mitochondrial dysfunction or mitochondrial deficiencies, and cosmetics, for instance to prevent or delay skin aging.

- **Title: Hydroxybenzoic acid derivatives, methods and uses thereof**

Publication number: WO2018122789 (A1); International Application: PCT/IB2017/058508
Publication date: 05.07.2018

Authors: Maria Fernanda Martins Borges, Paulo Jorge Gouveia Simões da Silva Oliveira, José Carlos Santos Teixeira, Fernando Cagide Fagin, Ana Catarina Gomes Oliveira
Entity: Universidade do Porto & Centro de Neurociências e Biologia Celular

Abstract
The present disclosure relates to the design and synthesis of new mitochondriotropic antioxidant compounds based on hydroxybenzoic acids and analogues. Furthermore, this disclosure is also related to the methods and uses of the hydroxybenzoic based derivatives and analogues, for example, in the field of human and animal diseases, for instance to treat mitochondrial dysfunction or mitochondrial deficiencies, and cosmetics, for instance to prevent or delay skin aging.

The expenses of the two patents are being supported by two approved projects of P2020|COMPETE (Aviso 17/SI/2015 and Aviso 04/SIAC/2017)

2.1.7. Technology Transfer

The two patents «Hydroxycinnamic derivatives, methods and uses thereof» (PCT/IB2017/056412) and «Hydroxybenzoic derivatives, methods and uses thereof (PCT/IB2017/058508)» have been licensed to MitoTAG, a spin-off co-founded by the task coordinator F Borges to exploit their commercial applications for cosmetics, human health and veterinary (http://www.mitotag.com/).

2.1.8. Divulgação

Link de videos
https://upin.up.pt/pt-pt/content/inventores-fernanda-borges
Porto Canal. Minuto 10:15 http://videos.sapo.pt/FQ1YzmuYyW5fKH6ZZGev

2.1.9. Conclusions

Innovative, potent and safe biobased antioxidants have been successfully developed. The health promoting effects and safety profile of some Bioantioxidants has been evaluated. The new chemical entities can be used, in a next future, either as additives or active packaging films or for health application in the prevention and/or therapy of oxidative stress-related diseases (functional foods, nutraceuticals or health products).
The optimization of the properties of the most relevant systems has been successfully performed by structural and physicochemical relationship (SPR) studies. Bioavailability or physicochemical drawbacks have been circumvented by the development of new nanoengineered solutions.
As BIOANTIOX project could create novel industry application (on a tangible environment) and commercial opportunities the best candidates that successfully overcome the requirements have been transferred to the spin–off MitoTAG that will work as a bridge between academia and Industry.
The evaluation of the effect of some bio-based antioxidants on oxidation stability of diverse industry matrices is still in progress. The follow-on data will be published in the next few months.

2.2 Research Task: 2 - NANODEL: Smart Nanosystems for Controlled Delivery

Responsible Scientist: Prof Doutor Eduardo Jorge Figueira Marques

Goals:
i) Development of novel stimuli-responsive liposomes for drug and gene delivery
ii) Study of antimicrobial peptide immobilization and delivery from self-assembled nanotubes.
iii) Preparation and characterization of responsive polymer-based nanoparticles and nanogels
iv) Study of intermolecular interactions and energetics of solvation with relevance to drug binding

2.2.1. Description of activities and results

1. Catanionic liposome and micellar systems based on single surfactants and gemini surfactants have been characterized [publications 1-4]. Ultra small lipid nanoparticles containing cationic surfactants were investigated, showing good potential for site-specific drug delivery for glioblastoma treatment [publication 5]. Charge and pH-tunable serine-based catanionic liposomes were tested in vitro for the delivery of the anticancer drug doxorubicin, revealing good results in release profiles and cell uptake [publication 6]. Studies in cell viability of catanionic vesicles based on commercial and amino acid surfactants were performed (master thesis in september 2019). Different families of gemini surfactants were studied regarding their efficiency to complex and deliver genetic material in human cell lines (manuscript soon to be submitted). A new line of work concerning the development of photoresponsive liposomes was started and developed with relevant results.

- The study of antimicrobial peptides (AMPs) and their action/mechanisms in solution, in order to ascertain differences in activity and specificity, has been carried out [publications 7 and 8]. Five different antimicrobial peptides (D,L-cyclic peptides of planar conformation) were extensively studied. These peptides form self-assembling cyclic peptide nanotubes (SCPNs) when in contact with membranes. The interaction of these cyclic antimicrobial peptides (provided by Prof. Juan Granja, Santiago de Compostela, Spain) with model membranes (liposomes, Large Unilamellar Vesicles, LUVs) of different compositions was assessed by DSC as a first approach technique and complemented with structural data from Molecular Dynamics (MD), ATR-FTIR, and Solid State NMR (at Martin Luther University Halle-Wittenberg, Germany), as well as membrane partition from fluorescence studies (static and time resolved (this in Prof Manuel Prieto's lab, IST, Lisboa). Many results were obtained, the first paper will be submitted in September 2019, the second is aimed at November 2019, and the third in January 2020. The work was presented in 6 international conferences, as Oral communications and poster presentations.

- Two new lines of work were initiated and developed: i) the formation of lipid nanodiscs using special polymers of SMA and DIBMA type and ii) the use of these lipid nanodiscs to assess the role of lipids in synuclein aggregation and function, and to characterize lipid-induced aggregation. A large number of results were obtained for i) for different lipid systems by a Master student. As regarding ii), the results were outstanding, leading to the proposal of a new application of the newly discovered copolymer/lipid nanodiscs, as an excellent tool to study secondary structure formation and for preventing toxic aggregation (paper submitted).

- The development and characterization of polymer/surfactant microgels derived from the anionic lysine-based gemini and cationic hydroxyethylcellulose derivatives were completed (manuscript under submission). Further studies were undertaken regarding lysine-based nanogels in terms of their cytotocity, and ability to encapsulate model bioactive molecules (2 manuscripts under prepararion for 2019 and 2020).

- The development of pegylated nanoplatforms for targeted brain delivery has been realized. The smart carriers has been used to deliver bioactive molecules (e.g.coumarin C75 and chromone C27), in the context of the treatment of neurodegenerative diseases and HIV [publications 9, 10 e 11].

- Extensive work on the enthalpies of solvation of alcohols in ionic liquids was carried out [publication 12]. Experimental and theoretical approaches were used to the study the solvation of alcohols in ILs with different combinations of anion and cation leading to insights into the preferential location of the alcohol and intermolecular interactions established with ILs.

- Self-assembled nanotubes formed by lysine-based surfactant with strong temperature and pH-sensitive dependence, have been extensively studied using a comprehensive toolbox (SEM, TEM, SAXS and DSC) [publication 13]. The effect of different buffers and biological fluids on nanotube formation and morphology, cell viability, and protein loading have been performed. Further results are in the course of publication.

2.2.2.Deviations from the approved project

No significant deviations occurred with respect to the workplan. All four sub-tasks were actively developed and results are available for all of them. Most of the activities and results have focused on goals (i) and (ii) and several publications were obtained and are foreseen for the near future. Goals (iii) and (iv) were reinforced in last part of the project.

2.2.3. Scientific Publications

Book chapters

1. Design and Applications of Cyclic Peptides
   in Applications in Biomedicine, Biotechnology and Bioengineering
   Claro, B.; Bastos, M.; Garcia-Fandino, R. (2017), Ed. Sotirios Koutsopoulos, Elsevier.

Articles

1. Ferreira, J.; Mikhailovskaia, A.; Chenneviere, A; Restagno F.; Cousin, F.; Muller, F; Degrouard, J.; Salonen, A.; Marques E.F. Interplay between bulk self-assembly, interfacial and foaming properties in a catanionic surfactant mixture of varying composition. *Soft Matter* **2017**, *13*, pp. 7197-7206. http://pubs.rsc.org/en/content/articlepdf/2017/SM/C7SM01601H.

2. Fernandes, R.M.F.; Wang,Y.; Tavares, P.; Nunes, S; Pais, A.A.C.C.; Marques E.F. Critical role of the spacer length of gemini surfactants on the formation of ionic liquid crystals and thermotropic behavior. *J. Phys. Chem. B* **2017**, *121*, pp. 10583-10592. https://dx.doi.org/10.1021/acs.jpcb.7b08618.

3. Vicente, F.; Cardoso, I.; Sintra, T.; Lemus, J.; Marques, E.F.; Ventura, S.; Coutinho, J.A.P. The impact of surface-active ionic liquids on the cloud points of nonionic surfactants and the formation of aqueous micellar two-phase systems. *J. Phys. Chem. B* **2017,** *121*, pp. 8742-8755. https://dx.doi.org/10.1021/acs.jpcb.7b02972.

4. Wang, Y.; Fernandes, R.F.M.; Marques, E.F. From single gemini surfactants in water to catanionic mixtures with the bile salt sodium taurodeoxycholate: Extensive micellar solutions,coacervation and liquid crystal polymorphism as revealed by phase behavior studies. *J. Mol. Liq.* **2019**, *285*, pp. 330–337. https://doi.org/10.1016/j.molliq.2019.04.067

5. Mendes, M.; Miranda, A.; Cova, T.; Gonçalves, L.; Almeida, A.J.; Sousa, J. J.; Vale, M.L.C.; Marques, E.F.; Pais, A.; Vitorino, C. Modeling of ultra-small lipid nanoparticle surface charge for targeting gliobastoma. *Eur. J. Pharm. Sci*. **2018**, *117*, pp. 255-269. https://doi.org/10.1016/j.ejps.2018.02.024

6. Lopes, R.C.F.G.; Silvestre, O.F.; Faria, A.R.; Vale, M.L.; Marques, E.F., Nieder J., Surface charge tunable catanionic vesicles based on serine-derived surfactants as efficient nanocarriers for the delivery of the anticancer drug doxorubicin. *Nanoscale* **2019**, *11*, pp. 5932–5941. https://doi.org/10.1039/C8NR06346J

7. Silva, T.; Claro, B.; Silva, B.F.B.; Vale, N.; Gomes, P.; Gomes, M.S.; Funari, S.S.;Teixeira, J.; Uhríková, D.; Bastos, M. Unravelling a mechanism of action of a cecropin A-melittin hybrid antimicrobial peptide – the induced formation of multilamellar lipid stacks. *Langmuir* **2018**, *34*, pp. 2158−2170. https://dx.doi.org/10.1021/acs.langmuir.7b03639

8. Piñeiro, A.; Muñoz, E.; Sabín, J.; Costas, M.; Bastos, M.; Velázquez-Campoy, A.; Garrido, P.F.; Dumas, P.; Ennifar, E.; García-Río, L.; Rial, J.; Pérez, D.; Fraga, P.; Rodríguez, A.; Cotelo, C. AFFINImeter: A software to analyze molecular recognition processes from experimental data. *Anal. Biochem.* **2019**, *577*, pp. 117-134. https://doi.org/10.1021/acscentsci.8b00362

9. Fernandes, C.; Martins, C.; Fonseca, A.; Nunes, R.; Matos, M.J.; Silva, R.; Garrido, J.; Sarmento, B.; Remião, F.; Otero-Espinar, F.; Uriarte, E.; Borges, F. PEGylated PLGA Nanoparticles as a Smart Carrier to Increase the Cellular Uptake of a Coumarin-Based Monoamine Oxidase B Inhibitor. *ACS Appl. Mater. Interfaces* **2018**, *10*, pp. 39557-39569. https://dx.doi.org/10.1021/acsami.8b17224.

10. Pinto, M.; Fernandes, C.; Martins, E.; Silva, R.; Benfeito, S.; Cagide, F.; Mendes, R. F.; Paz F.A.A.; Garrido J.; Remião, F.; Borges, F. Boosting Drug Discovery for Parkinson´s: Enhancement of the Delivery of a Monoamine Oxidase-B Inhibitor by Brain-Targeted PEGylated PCL-based Nanoparticles. *Pharmaceutics* **2019**, *7*, pp. 331-352. https://doi.org/10.3390/pharmaceutics11070331.

11. Martins, C.; Araújo, F.; Gomes, M. J.; Fernandes, C.; Nunes, R.; Li, W.; Santos, H. A.; Borges, F.; Sarmento, B. Using microfluidic platforms to develop CNS-targeted polymeric nanoparticles for HIV therapy. *Eur. J. Pharm. Biopharm.* **2019**, *138*, pp. 111-124. https://doi.org/10.1016/j.ejpb.2018.01.014.

12. Vaz, I.CM.; Bastos, M.; Bernardes, C.E.S.; Canongia Lopes, J.N.; Santos, L.M.N.B.F. Solvation of Alcohols in Ionic Liquids – understanding the effect of the Anion and Cation. *Phys. Chem. Chem. Phys.* **2018**, *20*, pp. 2536-2548. https://dx.doi.org/10.1039/C7CP07525A.

13. Oliveira, I.S.; Lo, M.; Araújo, M.J.; Marques, E.F., Temperature-responsive self-assembled nanostructures from lysine-based surfactants with high chain length asymmetry: from tubules and helical ribbons to micelles and vesicles, *Soft Matter*, **2019**, *15*, pp. 3700-3711. https://doi.org/10.1039/c9sm00399a.

2.2.4. PhD Theses

In progress

1. Isabel Maria Santos da Costa Oliveira, Self-organized smart nanotubes for controlled delivery of antimicrobial peptides: an integrated approach,
   PhD thesis, University of Porto.
   Supervisor: E.F. Marques. Co-supervisor: A. Gomes (Univ. Minho).

2. Bárbara Maria Amaro Gonçalves Claro. Peptidomimetics as new antibiotic paradigm - a combined biophysical and MD approach,
   PhD Thesis, University of Porto.
   Supervisor: M. Bastos. Co-supervisor: Rebeca Garcia-Fandiño.

3. Raquel Cristina Fonseca Gonçalves Lopes, G2D – Gold-Graphene Dots: Fabrication, Characterization and Application in Bioimaging and Sensing,
   PhD Thesis, University of Porto.
   Supervisor: E.F. Marques. Co-supervisors: J.G. Martinho (IST-UL), E. Maçoas (IST-UL).

4. Catarina Dias da Costa, Cell-on-Cell: uma nova abordagem circular em nanotecnologias de base celulósica para promoção de repelência, amaciamento e superabsorção em têxteis
   PhD Thesis, University of Porto.
   Supervisor: E.F. Marques. Co-supervisors: N. Azoia (CeNTI), C. Silva (CeNTI).

2.2.5. Master Theses

Concluded

1. Ricardo Bessa, A biophysical approach to mitochondrial gene therapy: gemini surfactant-based colloidal vectors
   Master Thesis, University of Porto, 2016.
   Supervisor: E. F. Marques. Co-supervisor: A. Jurado (Univ. Coimbra).

2. José Ferreira, A biophysical approach to mitochondrial gene therapy: gemini surfactant-based colloidal vectors
   Master Thesis, University of Porto, 2016.
   Supervisor: E. F. Marques. Co-supervisor: A. Salonen (Univ. Paris-Sud).

3. Raquel Lopes. Biocompatibility and cell uptake studies of novel liposomes based on amino acid derived surfactants
   Master Thesis, University of Porto, 2017.
   Supervisor: E. F. Marques. Co-supervisor: J. Nieder (INL, Braga).

4. Filipe Coelho, Bulk and microfluidic-assisted preparation of bioreducible polyplexes for gene therapy,
   Master Thesis, University of Porto, 2017.
   Supervisor: E. F. Marques. Co-supervisor: B. Silva (INL, Braga).

5. Inês Martins, Caracterização de membranas modelo por DSC e estudo da partição de drogas para membranas por ITC
   Master Thesis, University of Porto, 2018.
   Supervisor: M. Bastos.

6. Inês Garrido, Formação de nano-discos lipídicos através de SMALPs para isolamento de proteínas membranares no seu envelope lipídico natural
   Master Thesis, University of Porto, 2019.
   Supervisor: M. Bastos. Co-supervisor: M. J. Moreno (Univ. Coimbra).

7. Karenina Santos, Vesículos cataniónicos - caracterização estrutural, avaliação toxicológica e estudos de encapsulação de biomoléculas
   Master Thesis, University of Porto, 2019.
   Supervisor: E. F. Marques. Co-supervisor: A. Gomes (Univ. Minho).

2.2.6. Patents

2.2.7. Conclusions

The preparation, characterization and functionalization of different nano-structured systems for the loading, transport and smart delivery of biomolecules were undertaken according to the initial workplan. Liposomes, self-assembled chiral nanotubes, micellar systems and solid nanoparticles were developed for a wide range of bioactive molecules, such as AMPs, cancer drugs, genes and antioxidants. Among the most significant achievements, we highlight two: (i) the development of biocompatible catanionic vesicles based on serine-derived surfactants that were shown to be highly effective *in vitro* in the phase delivery of the anticancer drug doxorubicin to cancer lung cells, paving the way to further optimization this system and in several catanionic vesicles that are being developed; (ii) the use of lipid nanodiscs to assess the role of lipids in synuclein aggregation and function, and the in-depth characterize of the lipid-induced aggregation.
The four main goals that were planned have thus all been successfully developed. The scientific results and achievements for each goal were obtained. Regarding the scientific publications of the Nanodel Task overall, several papers were published in the course of the project and at least 10 more manuscripts are either submitted or near submission, with the expectation to be published in the next few months.

2.3 Research Task: 3 - FUNCOAT: Functional nanocoatings

Responsible Scientist: Prof Doutor António Fernando Sousa da Silva

Goals:
i) High quantum yield carbon upconversion nanoparticles for analytical sensing.
ii) Coating materials based on cork and inorganic nanomaterials.
iii) Hollow nanostructured-shell titania microspheres for selective photocatalysis.
iv) Functional surfaces prepared by electrodeposition from ionic liquids.
v) Functional surfaces prepared by electrochemical polymerization or copolymerization.
vi) Novel pH-sensitive and oxidation-"activatable" nanomaterials based on coelenterazine/ polymeric micelles nanoconjugates.

2.3.1. Description of activities and results

1 High quantum yield carbon upconversion nanoparticles for analytical sensing.

Several carbon-based nanomaterials (carbon dots) were synthesized from different precursors through hydrothermal and microwave techniques. Their properties were then modified through doping strategies with different heteroatoms and coating with appropriate molecules. The carbon dots were analyzed through different structural and morphological characterization techniques (SEM / TEM, infrared, dynamic light scattering and XPS). Finally, these carbon dots were successfully applied as optical fluorescence sensors for the detection and quantification of compounds of interest (such as reactive oxygen species and carbohydrates).

Upconversion nanomaterials were synthesized from rare-earth metals via either the hydrothermal or co-precipitation synthesis route, followed by appropriated doping strategies. These nanomaterials were characterized by SEM, infrared, XRD, XPS and dynamic light scattering. Their ability to upconvert infrared radiation into visible light was applied to nanothermometry and security applications.

2 Coating materials based on cork and inorganic nanomaterials. 2.1. Evaluation of the carbon footprint of cork products

The carbon footprint of a cork board (ICB) of a Portuguese company was evaluated through a life cycle analysis. It has been shown to have a negative footprint due to the use of cork, a renewable raw material. Comparison with other commercial products showed the superiority of ICBs from a carbon footprint point of view.

2.2. Development of new wood coatings

It was developed two novel types of coatings for wood products. One of the them consists on a formulation composed of phosphorescent oils and phosphors has been developed to coat wood products, whose main property is the emission of light after exposure to natural and artificial light. The second type of coating is composed by nanostructured photonic crystals, which provides iridescent properties to wood.

3 Hollow nanostructured-shell titania microspheres for selective photocatalysis.

Due to the need of integration with other tasks (namely BIOANTIOX) the work was focused in the use of mesoporous silica nanoparticles since these are more promising.

Nevertheless, TiO_2-based nanomaterials were successfully synthesized by doping TiO_2 with Co, Mn, and Ni and by co-doping it with (P,Mo) or (P,W). The structural, optical, and morphological properties of the synthesized nanomaterials have been investigated by XRD, FTIR, UV-Vis diffuse reflectance, SPX and SEM-EDS. The obtained photocatalytic activity for the degradation

of model pollutants (under visible light) showed that both mono-doping of TiO_2 with Co and its co-doping with (P,Mo) or (P,W) improve significantly the photocatalytic activity of these materials.

4 Synthesis and optimization of mesoporous silica nanoparticles

4.1 The mesoporous silica nanoparticles (MSiNP) were synthesized at room temperature by sol-gel methodology via hydrolysis and condensation of the precursor, tetraethylorthosilicate (TEOS), using N-cetyltrimethylammonium bromide (CTAB) as porous mold and NH_3 as catalytic agent. To maximize the yield of nanoparticle synthesis with a minimum of experiments, a factorial planning approach. The influence of the concentration of TEOS, CTAB and NH_3 on the particle properties was evaluated through a factorial planning 32 with triplicate of central point, composed of 3 variables that were defined in 3 levels each.

4.2 For coating MSiNP, 100 mg of nanoparticles were added and homogenized by magnetic stirring with a solution of 60,000 PVA (10 mL, 5%, m / v) for 7 h at room temperature. The suspension was centrifuged (6000 rpm / 20 °C, 10 min), washed twice with water and dried at 65 ° C for 1 h.

For encapsulation of caffeic acid in MSiNP-PVA, 100 mg of coated nanoparticles were incubated in 10 mL of ultrapure water containing 5.2 mg / mL of caffeic acid under magnetic agitation (150 rpm, 24 h) and centrifuged (6000 rpm, 10 min, 20ºC). The pellets were dried at 65 ºC / 1 h and stored at 5 ºC until needed.

4.3 Fe_3O_4 nanoparticles synthesized by a co-precipitation of co-Fe^{+2} and Fe^{+3} solutions under alkaline conditions. Briefly, 1.99 g (10 mmol) of $FeCl_2.4H_2O$ and 3.24 g (12 mmol) of $FeCl_3.6H_2O$ dissolved in 50 mL of distilled water. A separate NH_3 solution was made by dissolving 30 mL NH3 (32% ammonia) in 50 mL distilled water. Both solutions allowed stirring for about half an hour to achieve uniform mixing. Soon after, the NH_3 solution added dropwise to the first solution to a pH of 9. The precipitates were separated with the help of an external magnet, washed with distilled water and ethanol, and dried at 120 °C overnight and then shredded to form finally the black magnetic NPs.

4.4 Structured Fe_3O_4@ MCM-41 prepared using the magnetites as nuclei by the Stöber method. Briefly, 0.5 g Fe_3O_4 dispersed in a solution composed of 60 mL ethanol and 120 mL deionized water. The resulting mixture homogenized by ultrasound for 30 min, and then 1.2 mL of aqueous ammonia solution introduced into the solution and allowed to stir for 1h. Subsequently, a dropwise added CTAB solution (100 mmol / L) added, which acts as a targeting agent to form the structure of the MCM-41. To this homogeneous solution, TEOS (2 mL) added dropwise and the reaction mixture stirred slowly for 24h. The solid products were separated by external magnet and washed three times with an ethanol/deionized water mixture. Finally, the product was oven dried at 60 °C for 24h and calcined at 550 °C for 4h.

5 Effectiveness studies of caffeic acid encapsulation in silica nanoparticles

At low pH (pH 1.2), there was slower release of caffeic acid compared to the release at pH 6.8 and 7.4. The results showed that the amount of caffeic acid released at pH 1.2 after 120 min was 73%, while after 30 min almost all caffeic acid was released. At pH 1.2, the low release of caffeic acid can be attributed to the interaction between caffeic acid and the silanols groups by hydrogen bonds. As silica pI is close to 2.0 and the pKa of caffeic acid is 4.62, at pH 1.2 the OH groups of caffeic acid are protonated. On the other hand, at pH 6.8 and 7.4, the OH groups of the silanols and the caffeic acid are deprotonated and therefore there is a repulsive force between them and a high amount of caffeic acid is released.

These studies were also performed with the magnetic Fe_3O_4@ MCM-41 nanomaterials. A slower release with a sustained rate is observed with a percentage ranging from 26.95 to 63.01 %, with

this high rate in the first 30 minutes caused by rapid diffusion of caffeic acid into buffered or non-adsorbed medium surface.

6 Eco-toxicological studies of nanoparticles and caffeic acid

The comparative toxicity of the nanoparticles and caffeic acid was evaluated using the microalgae R. subcapitata, growth of L. minor aquatic plants.

MSiNP and MSiNP loaded with caffeic acid decreased the algae growth rate only at the highest concentration (25 mg / L). The mean particle size in MBL was similar for both nanoparticles (MSiNP and MSiNP-AC) (≈ 100 nm) and the absence of algal toxicity may be due to the low surface area of the nanoparticles, thus reducing contact between the particles and the algae. In the presence of the MSiNP no signs of growth inhibition were observed when the plants were exposed to concentrations of 3.3 to 25 mg / L after 7 days. No significant differences were found in the number of leaves as well as in the dry weight between the control group and the plants exposed to nanoparticles. Thus, there was no effect of MSiNP on L. minor plants.

All tested NPS were also toxic to L. minor, contributing for a significant reduction ($p<0.5$) in the growth rate. Fe_3O_4@MCM-41 was the most toxic NPS and significantly reduced ($p<0.5$) the Lemna growth rate at the lowest tested concentration 52.7 mg / L, in a dose dependent manner, showing an EC50 value of 247.7 mg / L.

The toxicity towards V. fischeri (Microtox® assay) of NPs decreased with exposure time and an EC20 of 146 and 438.8 mg /L after 30 min were recorded, respectively. Nanomaterials coated with were less toxic to the bacteria, and toxicity greatly decrease with exposure time.

7 Functional surfaces prepared by electrodeposition from ionic liquids

Room temperature ionic liquids and an alternative special kind of "ionic liquids", the deep eutectic solvents (DES) were used as templates in the synthesis of mesoporous silica. The most common DES are comprised of choline chloride and a neutral hydrogen bond donor that forms a Lewis aduct with chloline, and are in use in our labs for some time already. Although there was no previous evidence that DES would play a mesoporous templating action, moreover in more complex mixtures than those used in purely sol-gel synthesis, the advantages presented by the choline-based DES over traditional ionic liquids are huge and justified our option. DES are much cheaper than the most important ionic liquids, easily prepared in-house (no purification, no waste disposal) from safe, common reagents and are inert to water (long term stability, easy

storage). To the best of our knowledge, this work presents the first utilization of DES for the purpose of mesoporosity development.

8 Functional surfaces prepared by electrochemical polymerization or copolymerization The work performed consisted in the electropolymerization, on a gold screen-printed electrode (Au-SPE) and on the SPR gold sensor, of poly-pyrrole (p-Py).

The use of Py generated highly selective printed materials for a protein and thus improve biosensor performance. CA-125 was covalently attached to the Au-SPE film, previously treated with cysteamine (Cys). SPR is a label-free and non-destructive optical technique providing high-quality data on CA-125 MIP binding interactions in real time at a conductive interface. In this study, the several steps involved in the molecular imprinting process, such as the template construction, the removal of the printed molecules from the polymer matrix and the rebinding of the template molecules to the polymer were followed using SPR reflectivity measurements. The detection of the CA-125 protein directly grafted on the SPR sensing chip was tracked based on the changes in the dielectric permittivity and the shift in the resonant angle of incidence of the sensor surface. A systematic investigation of several analytical parameters, such as sensitivity, dynamic linear range, limit of detection and selectivity, in order to evaluate the performance of the CA-125 electrochemical and optical biosensor, were also performed.

The protein imprinted poly(Toluidine Blue) film was grown in a pre-formed Toluidine Blue (TB) tailed SAM at the AuSPE surface, which greatly enhanced the stability against degradation of the Molecular Imprinted Polymer (MIP) film at the electrode surface.

The MIP receptor film recognition ability towards the protein was investigated by fitting data to Freundlich isotherm. The binding affinity (KF) obtained for the MIP system was significantly higher (~ 12-fold) to that obtained for the NIP system, demonstrating the success of the approach in creating imprinted materials that specifically respond to CA 15-3 protein.

The incubation of the MIP modified electrode with increasing concentration of protein (from 0.10 U / mL to 1000 U / mL) resulted in a decrease of the ferro/ferricyanide redox current. The device displayed linear response from 0.10 U / mL to 100 U / mL and LODs below 0.10 U / mL were obtained from calibration curves built in neutral buffer and diluted artificial serum, using DPV technique, enabling the detection of the protein biomarker at clinically relevant levels. The developed MIP biosensor was applied to the determination of CA 15-3 in spiked serum samples with satisfactory results.

9 Novel pH-sensitive and oxidation- “activatable” nanomaterials based on coelenterazine/polymeric micelles nanoconjugates

Elucidation of chemiluminescent reactions

A set of spectroscopic and theoretical techniques was used to elucidate the chemiexcitation mechanism of chemiluminescent systems, namely the class of marine imidazopyrazinones. The kinetic and energy profiles of the chemiluminescent reactions were obtained in pH solutions, allowing to determine a pronounced effect of the pH on the resulting light emission. The use of theoretical calculations at the DFT level allowed assigning this phenomenon to the neutral-anionic chemical balance of a dioxetanone intermediate. At acid pH, this intermediate is in its neutral form. During its thermolysis, the neutral dioxetanone enters a biradicalar region of its potential energy surface, where the fundamental and excited states are degenerate. This allows a transition from ground state to an excited state with high efficiency. For its part, at basic pH the dioxetanone is in its anionic form. The thermolysis of this species also gives access to a biradicalar region, but the fundamental and excited states are not degenerate, which leads to a lower chemiexcitation efficiency. Moreover, the theoretical calculations allowed to relate the presence

of the degeneration region with a greater electrostatic interaction between the dioxetanone fragments, which allows the planning of changes to dioxetanone for a more efficient chemiexcitation.

Such information allowed the rational design and subsequent synthesis of tumor-selective and self-activating photosensitizers based on chemiluminescent imidazopyrazinones. Such molecules were found to produce the highly reactive singlet oxygen as the result of a chemiluminescent reaction triggered by a tumor marker. Cytotoxicity assays demonstrated that the novel photosensitizers induced significant toxicity toward tumor cells, even better than reference drugs, while not inducing toxicity toward normal cells. This work provides a proof-of-concept for a novel type of photosensitizer that eliminates the current restrictions that photodynamic therapy presents regarding tumor size and localization.

10 Characterization of the photoacidity of chromophores

Steady-state and time-resolved spectroscopic techniques were used to study the photophysics and photochemistry of different photoacids. This allowed us to determine the radiative and non-radiative ratios, and to quantify their acidity in the excited state. The use of theoretical calculations allowed us to identify the deactivation and proton transfer pathways in the excited state.

11 Use of computational calculations in the study of environmentally-relevant processes

Computational computations at the DFT level were made to study the effect of organic aerosols on climate change, and to characterize the catalytic effect of organocatalysts on the conversion of CO2. In particular, the light-absorbing properties in the atmosphere of catechol and polycyclic aromatic hydrocarbons (and respective derivatives) have been studied. Both the spectra areas in which these compounds absorb sunlight and the strength of absorption have been identified. This type of information is essential for the development of accurate models for radiative forcing.

The epoxy ring opening reaction is a key step in the conversion reaction of CO2 into value-added products. A combined theoretical and experimental approach was used to determine the effect of hydrogen-bond donors (HBDs) as co-catalysts. It was found that HBDs present only a small effect on the activation energy. Furthermore, it was found that water molecules can act as HBDs with similar results to those provided by other organic molecules. Further work revealed that the activation energy is mainly determined by steric contributions.

12 Study of the degradation of UV filters

High-performance liquid chromatography (HPLC) was used to observe the degradation reactions of the 3-methylbutyl- (2E) -3- (4-methoxyphenyl) acrylate (IMC) UV filter, determine its degradation kinetics, and study the effect of external variables on their degradation. BMI undergoes degradation rapidly when exposed to free chlorine. However, BMI seems to be quite stable when exposed to solar radiation.

13 Study of the effect of atmospheric pollution on the properties of pollen

The effects of two atmospheric pollutants (O3 and NO2) on the allergenic properties and chemical composition of pollen samples were studied. The analyses showed changes in the allergenic properties of the pollen, being these different according to the pollutant tested. In addition, it has also been seen that the same pollutant can interact differently with each specific allergen. Finally, analysis by spectroscopy revealed structural changes in the pollen samples after exposure to atmospheric pollutants.

2.3.2. Deviations from the approved project

No deviations are reported

2.3.3. Scientific Publications

Edited Books

1. Pinto da Silva, L., Ed. In A Comprehensive Guide to Chemiluminescence; Nova Science Publishers, 2019; ISBN: 978-1-53616-170-0.

Book chapters

1. Núnez-Montenegro, A.; Ferreira, P.J.O., Pinto da Silva, L. Chemiluminescent Imidazopyrazinones: A Step to Future Diagnosis Tools. In A Comprehensive Guide to Chemiluminescence; Pinto da Silva, L., Ed.; Nova Science Publishers, 2019; Chapter 1. ISBN: 978-1-53616-170-0.

2. Pinto da Silva, L.; Magalhães, C.M.; Ferreira, P.J.O.; Crista, D.M.A. Chemi- and Bioluminescence in Self-Illuminating Photodynamic Therapy. In Photodynamic Therapy (PDT): Principles, Mechanisms and Applications. Fitzgerald, F., Ed.; Nova Science Publishers, 2017; Chapter 3. ISBN: 978-1-53611-912-1.

Articles

1. Pinto da Silva, L.; Núnez-Montenegro, A.; Magalhães, C.M.; Ferreira, P.J.O.; Duarte, D.; González-Berdullas, P.; Rodríguez-Borges, J.E.; Vale, N.; Esteves da Silva, J.C.G. Single-molecule chemiluminescent photosensitizer for a self-activating and tumor-selective photodynamic therapy of cancer. *Eur. J. Med. Chem.* **2019**, *183*, pp. 111683.

2. Pinto da Silva, L.; Magalhães, C.M.; Núnez-Montenegro, A.; Ferreira, P.J.O.; Duarte, D.; Rodríguez-Borges, J.E.; Vale, N.; Esteves da Silva, J.C.G. Study of the Combination of Self-Activating Photodynamic Therapy and Chemotherapy for Cancer Treatment. *Biomolecules* **2019**, DOI: 10.3390/biom9080384.

3. Sendão, R.M.S.; Crista, D.M.A.; Afonso, A.C.P.; Martínez de Yuso, M.V.; Esteves da Silva, J.C.G.; Pinto da Silva, L. Insight into the hybrid luminescence showed by carbon dots and molecular fluorophores in solution. *Phys. Chem. Chem. Phys.* **2019**, DOI: 10.1039/C9CP03730F [Epub].

4. Sampaio-Dias, I.E.; Silva-Reis, S.C.; Pinto da Silva, L.; García-Mera, X.; Maestro, M.A.; Rodríguez-Borges, J.E. Mechanistic insights for the transprotection of tertiary amines with Boc_2O *via* charged carbamates: access to both enantiomers of 2-azanorbornane-3-*exo*-carboxylic acids. *Org. Chem. Front.* **2019**, DOI: 10.1039/C9QO00957D [Epub].

5. Sousa, J.; Pinto da Silva, L. Modelling the absorption properties of polycyclic aromatic hydrocarbons and derivatives over three European cities by TD-DFT calculations. *Sci. Total Environ.* **2019**, *695*, pp. 133881. DOI: 10.1016/j.scitotenv.2019.133881.

6. Kumar, A.; Pinto da Silva, L.; Esteves da Silva, J.C.G.; Kumar, K. Molecular vibration assisted triplet-triplet annihilation nir-upconversion luminescence of fluorescein. *Opt. Mater.* **2019**, *96*, pp. 109286. DOI: 10.1016/j.optmat.2019.109286.

7. Rahmouni, A.; Saidi, R.; Khaddor, M.; Pinto, E.; Esteves da Silva, J.C.G.; Maouni, A. Chemical composition and antifungal activity of five essential oils and their major componentes against *Fusarium oxysporum* f. sp. *Albedinis* of Moroccan palm tree. *Euro-Mediterr. J. Environ. Integr.* **2019**, *4*, pp. 27. DOI: 10.1007/s41207-019-0117-x.

8. Mazivila, S.J.; Ricardo, I.A.; Leitão, J.M.M.; Esteves da Silva, J.C.G. A review on advanced oxidation processes: From classical to new perspectives coupled to two- and multi-way calibration strategies to monitor degradation of contaminants in environmental samples. *Trends Environ. Anal.* **2019**, *24*, pp. E00072. DOI: 10.1016/j.teac.2019.e00072.

9. Kumar, A.; Tiwari, S.P.; Kumar, K.; Esteves da Silva, J.C.G. Multifunctional applications of $NaGdF_4$:Ho^{3+}/Yb^{3+} upconversion phosphor synthesized via two different routes: a comparative study. *Mater. Res. Express* **2019**, *6*, pp. 106201. DOI: 10.1088/2053-1591/ab399c.

10. Maurya, S.K.; Kushawaha, R.; Tiwari, S.P.; Kumar, A.; Kumar, K.; Esteves da Silva, J.C.G. Thermal decomposition mediated Er^{3+}/Yb^{3+} codoped $NaGdF_4$ upconversion phosphor for optical thermometry. *Mater. Res. Express* **2019**, *6*, pp. 086211. DOI: 10.1088/2053-1591/ab20b4.

11. Pinto da Silva, L. Mechanistic study of the role of hydrogen bond donors in the two-component organocatalysis of the ring-opening reaction of epoxides. *Mol. Catal.* **2019**, *474*, pp. 110425. DOI: 10.1016/j.mcat.2019.110425.

12. Mello, G.P.C.; Simões, E.F.C.; Crista, D.M.A.; Leitão, J.M.M.; Pinto da Silva, L.; Esteves da Silva, J.C.G. Glucose Sensing by Fluorescent Nanomaterials. *Crit. Rev. Anal. Chem.* **2019**, *10*, pp. 1-10. DOI: 10.1080/10408347.2019.1565984.

13. Crista, D.M.A.; Mello, G.P.C.; Shevchuk, O.; Sendão, R.M.S.; Simões, E.F.C.; Leitão, J.M.M.; Pinto da Silva, L.; Esteves da Silva, J.C.G.3-Hydroxyphenylboronic Acid-Based Carbon Dot Sensors for Fructose Sensing. *J. Fluoresc.* **2019**, *29 (1)*, pp. 265-270. DOI: 10.1007/s10895-018-02336-2.

14. Pinto da Silva, L.; Magalhães, C.M. Mechanistic insights into the efficient intramolecular chemiexcitation of dioxetanones from TD-DFT and multireference calculations. *Int. J. Quantum Chem.* **2019**, *119 (9)*, e25881. DOI: 10.1002/qua.25881.

15. Gajst, O.; Pinto da Silva, L.; Esteves da Silva, J.C.G.; Huppert, D. Enhanced Excited-State Proton Transfer via a Mixed Methanol-Water Molecular Bridge of 1-Naphthol-3,6-disulfonate in Methanol-Water Mixtures. *J. Phys. Chem. A* **2019**, *123 (1)*, pp. 48-58. DOI: 10.1021/acs.jpca.8b10374.

16. Magalhães, C.M.; Esteves da Silva, J.C.G.; Pinto da Silva, L. Comparative study of the chemiluminescence of coelenterazine, coelenterazine-e and Cypridina luciferin with an experimental and theoretical approach. *J. Photochem. Photobiol. B* **2019**, 190, pp. 21-31. DOI: 10.1016/j.jphotobiol.2018.11.006.

17. Mazivilla, S.J.; Castro, ERA.; Leitão, J.M.M.; Esteves da Silva, J.C.G. At-line green synthesis monitoring of new pharmaceutical co-crystals lamivudine:theophylline polymorph I and II, quantification of polymorph I among its APIs using FT-IR spectroscopy and MCR-ALS. *J. Pharm. Biomed. Anal.* **2019**, *169*, pp. 235-244. DOI: 10.1016/j.jpba.2019.03.014.

18. Algarra, M.; Bartolic, D.; Radotic, K.; Mutavdzic, D.; Pino-Gonzalez, M.S.; Rodríguez-Castellón, E.; Lázaro-Martínez, J.M.; Guerrero-González, J.J.; Esteves da Silva, J.C.G.; Jimenez-Jimenez, J. P-doped carbon nano-powders for fingerprint imaging. *Talanta* **2019**, *194*, pp. 150-157. DOI: 10.1016/j.talanta.2018.10.033.

19. Kumar, A.; Esteves da Silva, J.C.G.; Kumar, K.; Swart, H.C.; Maurya, S.K.; Kumar, P.; Tiwari, S.P. Improvement in upconversion/downshifting luminescence of Gd_2O_3:Ho^{3+}/Yb^{3+} phosphor through Ca^{2+}/Zn^{2+} incorporation and optical thermometry studies. *Mater. Res. Bull.* **2019**, *112*, pp. 28-37. DOI: 10.1016/j.materresbull.2018.11.031.

20. Kumar, A.; Tiwari, S.K.; Kumar, K.; Esteves da Silva, J.C.G. Magnetic tuning in upconversion emission enhanced through Ag^{+} ions co-doped in GdF_3:Ho^{3+}/Yb^{3+} phosphor and a real-time temperature sensing demonstration. *J. Alloys Compd.* **2019**, *776*, pp. 207-214. DOI: 10.106/j.jallcom.2018.10.156.

21. El Mragui, A.; Zegaoui, O.; Daou, I.; Esteves da Silva, J.C.G. Preparation, characterization, and photocatalytic activity under UV and visible light of Co, Mn, and Ni mono-doped and (P,Mo) and (P,W) co-doped TiO_2 nanoparticles: a comparative study. *Environ. Sci. Pollut. Res. Int.* **2019**. DOI: 10.1007/s11356-019-04754-6. [Epub ahead of print].

22. Santos, A.J.; Esteves da Silva, J.C.G. Environmental fate and behaviour of the UV filter and emerging pollutant benzophenone-8 in aqueous solution. *Environmental Technology & Innovation* **2019**, *10*, pp. 48-61. DOI: 10.1016/j.eti.2018.10.010.

23. Abhishek Kumar, A., Tiwarib, S.P., Swart, H.C., Esteves da Silva, J.C.G. Infrared interceded YF3: Er3+/Yb3+ Upconversion phosphor for crime scene and anti-counterfeiting applications. *Optical Materials* **2019**, *92*, pp. 347-351. DOI: 10.1016/j.optmat.2019.04.050.

24. Maurya, S.K.,Kushwaha, R., Tiwari, S.P., Kumar, A., Kumar, K., Esteves da Silva, J.C.G. Thermal Decomposition Mediated Er3+/Yb3+ Codoped NaGdF4 Upconversion Phosphor for Optical Thermometry. *Materials Research Express* **2019**, *6*, 086211. DOI: 10.1088/2053-1591/ab20b4.

25. Kumar, A.; Couto, M.H.M.; Tiwari, S.P.; Kumar, K.; Esteves da Silva, J.C.G. Effect of pH of Precursor on Up/Downconversion and Cathodoluminescence of Gd_2O_3:Ho^{3+}/Yb^{3+} Phosphor and Magneto-Optic Studies. *ChemistrySelect* **2018**, *3 (38)*, pp. 10566-10573. DOI: 10.1002/slct.201801556.

26. Pecelj, M.; Lukic, M.; Vucicevic, A.; Una-Alvarez, E.; Esteves da Silva, J.C.G.; Freinkina, I.; Ciganovic, S.; Bogdanovic, U. Geoecological evaluation of local surroundings for the purposes of recreational tourism. *J. Geogr. Inst. Jovan Cvijic SASA* **2018**, *68(2)*, pp. 215-231. DOI: 10.2298/IJGI1802215P.

27. Kumar, A.; Tiwari, S.P.; Sardar, A.; Kumar, K.; Esteves da Silva, J.C.G. Role of Ca^{2+} co-dopants on structural and optical properties of YF_3:Tm^{3+}/Yb^{3+} upconversion phosphor for improved thermometry. *Sens. Actuators A* **2018**, *280*, pp. 179-187. DOI: 10.1016/j.sna.2018.07.011.

28. Kumar, A.; Tiwari, S.P.; Esteves da Silva, J.C.G.; Kumar, K. Security writing application of thermal decomposition assisted $NaYF_4$:Er^{3+}/Yb^{3+} upconversion phosphor. *Laser Phys. Lett.* **2018**, *15(7)*, 075901. DOI: 10.1088/1612-202X/aab123.

29. Pereira, M.S.; Borges, A.C.; Heleno, F.F.; Faroni, L.R.D.; Esteves da Silva, J.C.G. Experimental Design Optimization of Dairy Wastewater Ozonation Treatment. *Water Air Soil Pollut.* **2018**, *229*, 74. DOI: 10.1007/s11270-018-3737-x.

30. Gajst, O.; Green, O.; Pinto da Silva, L.; Esteves da Silva, J.C.G.; Shabat, D.; Huppert, D. Excited-State Proton Transfer to H_2O in Mixtures of CH_3CN-H_2O of a Superphotoacid, Chlorobenzoate Phenol Cyanine Picolinium (CBCyP). *J. Phys. Chem. A* **2018**, *122 (41)*, pp. 8126-8135. DOI: 10.1021/acs.jpca.8b07591.

31. Gajst, O.; Pinto da Silva, L.; Esteves da Silva, J.C.G.; Huppert, D. Excited-State Proton Transfer from the Photoacid 2-Naphthol-8-sulfonate to Acetonitrile/Water Mixtures. *J. Phys. Chem. A* **2018**, *122 (30)*, pp. 6166-6175. DOI: 10.1021/acs.jpca.8b04417.

32. Gajst, O.; Pinto da Silva, L.; Esteves da Silva, J.C.G.; Huppert, D. Enhanced Excited-State Proton Transfer via a Mixed Water-Methanol Molecular Bridge of 1-Naphthol-5-Sulfonate in Methanol- Water Mixtures. *J. Phys. Chem. A* **2018**, *122 (20)*, pp. 4704-4716. DOI: 10.1021/acs.jpca.8b00957.

33. Min, C.G.; Liu, Q.B.; Leng, Y.; Huang, S.J.; Liu, C.X.; Yang, X.K.; Ren, A.M.; Pinto da Silva, L. Development of firefly oxyluciferin derivatives as pH sensitive fluorescent probes: A DFT/TDDFT study. *Comput. Theor. Chem.* **2018**, *1133*, pp. 18-24. DOI: 10.1016/j.comptc.2018.04.008.

34. Magalhães, C.M.; Esteves da Silva, J.C.G.; Pinto da Silva, L. Study of coelenterazine luminescence: Electrostatic interactions as the controlling factor for efficient chemiexcitation. *J. Lumin.* **2018**, *199*, pp. 339-347. DOI: 10.1016/j.jlumin.2018.03.069.

35. Pinto da Silva, L.; Green, O.; Gajst, O.; Simkovitch, R.; Shabat, D.; Esteves da Silva, J.C.G. Excited-State Proton Transfer of Phenol Cyanine Picolinium Photoacid. *ACS Omega* **2018**, *3(2)*, pp. 2058-2073. DOI: 10.1021/acsomega.7b01888.

36. Lourenço, J.M.; Esteves da Silva, J.C.G.; Pinto da Silva, L. Combined experimental and theoretical study of Coelenterazine chemiluminescence in aqueous solution. *J. Lumin.* **2018**, *194*, pp. 139-145. DOI: 10.1016/j.jlumin.2017.10.025.

37. Mazivilla, S.J. Trends of non-destructive analytical methods for identification of biodiesel feedstock in diesel-biodiesel blend according to European Commission Directive 2012/0288/EC and detecting diesel-biodiesel blend adulteration: A brief review. *Talanta* **2018**, *180*, pp. 239-247. DOI: 10.1016/j.talanta.2017.12.057.

38. Santana, F.B.; Mazivilla, S.J.; Gontijo, L.C.; Neto, W.B.; Poppi, R.J. Rapid Discrimination Between Authentic and Adulterated Andiroba Oil Using FTIR-HATR Spectroscopy and Random Forest. *Food Anal. Method.* **2018**, *11 (7)*, pp. 1927-1935. DOI: 10.1007/s12161-017-1142-5.

39. Mazivilla, S.J.; Bortolato, S.A.; Olivieri, A.C. MVC3_GUI: A MATLAB graphical user interface for third-order multivariate calibration. An upgrade including new multi-way models. *Chemom. Intell. Lab. Syst.* **2018**, *173*, 21-29. DOI: 10.1016/j.chemolab.2017.12.012.

40. Mazivilla, S.J.; Olivieri, A.C. Chemometrics coupled to vibrational spectroscopy and spectroscopic imaging for the analysis of solid-phase pharmaceutical products: A brief review on non-destructive analytical methods. *Trends Anal. Chem.* **2018**, *108*, pp. 74-87. DOI: 10.1016/j.trac.2018.08.013.

41. Ribeiro, J.; Benfeito, S.; Cagide, F.; Teixeira, J.; Oliveira, P. J.; Borges, F.; Silva, A. F.; Pereira, C. M. Electrochemical behavior of a novel mitochondria-targeted antioxidant at an ITIES: An alternative approach to study lipophilicity. *Anal. Chem.* **2018**, *90(13)*, pp. 7989-7996.

42. Rebelo, T.S.C.R.; Costa, R.; Brandão, A.T.S.C.; Silva A.F.; Sales, M.G.F.; Pereira, C.M. Molecularly imprinted polymer SPE sensor for analysis of CA-125 on serum. *Analytica Chimica Acta*, **2019**, *1082*, pp. 126-135. Doi: 10.1016/j.aca.2019.07.050

43. Min, C.G.; Pinto da Silva, L.; Esteves da Silva, J.C.G.; Yang, X.K.; Huang, S.J.; Ren, A.M.; Zhu, Y.Q. A computational investigation of the equilibrium constants for the fluorescent and chemiluminescent states of Coelenteramide. *ChemPhysChem* **2017**, *18*, pp. 117-123.

44. Pinto da Silva, L.; Pereira, R.J.; Magalhães, C.M.; Esteves da Silva, J.C.G. Mechanistic Insight into Cypridina Bioluminescence with a Combined Experimental and Theoretical Chemiluminescent Approach. *The Journal of Physical Chemistry B* **2017**, *121*, pp. 7862-7871.

45. Min, C.G.; Ferreira, P.J.O.; Pinto da Silva, L.; Theoretically obtained insight into the

mechanism and dioxetanone species responsible for the singlet chemiexcitation of Coelenterazine. *Journal of Photochemistry and Photobiology B - Biology* **2017**, *174*, pp. 18-26, 2017.

46. Pinto da Silva, L.; Theoretical Study of the Ring-Opening of Epoxides Catalyzed by Boronic Acids and Pyridinic Bases. *The Journal of Physical Chemistry C* **2017**, *121*, pp. 16300-16307, 2017.

47. Magalhães, A.C.O.; Esteves da Silva, J.C.G.; Pinto da Silva, L. Density Functional Theory Calculation of the Absorption Properties of Brown Carbon Chromophores Generated by Catechol Heterogeneous Ozonolysis. *ACS Earth and Space Chemistry* **2017**, *1*, pp. 353-360.

48. Pinto da Silva, L.; Pereira, R.F.; Esteves da Silva, J.C.G. Theoretical Analysis of the Effect Provoked by Bromine-Addition on the Thermolysis and Chemiexcitation of a Model Dioxetanone. *Journal of Chemistry* **2017** Vol. 2017, ID 1903981.

49. Pinto da Silva, L.; Magalhães, C.M.; Crista, D.M.A.; Esteves da Silva, J.C.G. Theoretical Modulation of singlet/triplet Chemiexcitation of Chemiluminescent Imidazopyrazinone dioxetanone via C8-substitution. *Photochemical & Photobiological Sciences* **2017**, 16, pp. 897- 907.

50. Pinto da Silva, L.; Simkovitch, R.; Huppert, D.; Esteves da Silva, J.C.G. Combined experimental and theoretical study of the photochemistry of 4- and 3-hydroxycoumarin. *Journal of Photochemistry and Photobiology A: Chemistry* **2017**, *338*, pp. 23-36.

51. Simões, E.FC.; Esteves da Silva, J.C.G.; Leitão, J.M.M. Peroxynitrite and Hypochlorite Fluorescence Quantification by S,N and P,N co-Doped Carbon Dots. *Current Trends in Analytical and Bioanalytical Chemistry* **2017**, *1*, pp. 9-20.

52. Simões, E.FC.; Leitão, J.M.M. ; Esteves da Silva, J.C.G. Sulfur and nitrogen co-doped carbon dots sensors for nitric oxide fluorescence quantification. *Analytica Chimica Acta* **2017**, *960*, pp. 117-122, 2017.

53. Santos, A.J.M.; Esteves da Silva, J.C.G. Fate and behaviour of the UV filter 3-methylbutyl-(2E)-3-(4-methoxyphenyl)-acrylate (IMC) in aqueous solution. *Journal of Environmental Chemical Engineering* **2017**, *5*, pp. 2469-2479.

54. Ribeiro, H.; Costa, C.; Abreu, I.; Esteves da Silva, J.C.G. Effect of O3 and NO2 atmospheric pollutants on Platanus x acerifolia pollen: Immunochemical and spectroscopic analysis. *Science of the Total Environment* **2017**, *599-600*, pp. 291-297.

55. Campos, B.B.; Mutavdzic, D.; Stankovic, M.; Radotic, K.; Lázaro-Martinez, J.M.; Esteves da Silva, J.C.G.; Contreras-Cáceres, R.; Pino-González, M.S.; Rodríguez- Castellón, E.; Algarra M. Thermo-responsive microgels based on encapsulated carbon quantum dots. *New Journal of Chemistry* **2017**, *41*, pp. 4835-4842.

56. Tártaro, A.S.; Mata, T.M.; Martins, A.A.; Esteves da Silva, J.C.G. Carbon footprint of the insulation cork board. *Journal of Cleaner Production* **2017**, *143*, pp. 925-932.

57. Campos, B.B.; Contreras-Cáceres, R.; Bandosz, T.J.; Jiménez-Jiménez, J.; Rodríguez-Castellón, E.; Esteves da Silva, J.C.G.; Algarra M. Carbon dots coated with vitamin B12 as selective ratiometric nanosensor for phenolic carbofuran. *Sensors and Actuators B: Chemical* **2017**, *239*, pp. 553-561.

2.3.4. PhD Thesis

Concluded

1. B.B. Campos, Dendrimer and Cadmium free Quantum dots Fluorescent Nanocomposites
   PhD Thesis, University of Porto, 2017.
   Supervisor: Joaquim C.G. Esteves da Silva. Co-supervisor: Manuel Algarra Gonzalez.

2. D. Pereira, Analysis of Phenolic, Sulfur and Volatiles Aroma Compounds in Wine of Fogo Island – Cape Verde
   PhD Thesis, University of Porto, 2017
   Supervisor: Joaquim C.G. Esteves da Silva.

3. E. Simões, Nanopartículas para a Deteção Luminescente em Fibra Óptica de Espécies Químicas de Oxigénio e Azoto
   PhD Thesis, University of Porto, 2017
   Supervisor: Joaquim C.G. Esteves da Silva. Co-supervisor: J.M.M. Leitão (U. Coimbra)

4. Albano Joel Santos, Investigation of the environmental fate of UV filters
   PhD Thesis, University of Porto, 2018
   Supervisor: Joaquim C.G. Esteves da Silva.

In progress

1. Vanessa R.A. Ferreira, Imprinted hollow TiO2 microspheres for selective photocatalysis
   PhD Thesis, University of Porto
   Supervisor: A. Fernando Silva. Co-supervisor: Manuel Azenha.

2. Sarmento Júnior Mazivila, Metodologias de deteção de fármacos antimaláricos e antisida
   PhD Thesis, University of Porto
   Supervisor: Joaquim C.G. Esteves da Silva.

3. Maria da Conceição Milhais Pinto Mendonça, Conceção, construção e avaliação de materiais de apoio para o ensino de Física e Química enculturados na realidade moçambicana - um estudo de caso de voluntariado internacional no âmbito da formação de professores.
   PhD Thesis, University of Porto
   Supervisor: Joaquim C.G. Esteves da Silva.

2.3.5. Patents

1 Patent pending (PPP59213) – Chemiluminescent imidazopyrazinone-based photosensitizers with available singlet and triplet excited states.
Authors: Pinto da Silva, L.; Núnez-Montenegro, A.; Esteves da Silva, J.C.G.; Borges, E.; Ferreira, P.J.O.; Crista, D.M.A.
Entity: Universidade do Porto.

2 Granted PCT (PCT/IB2014/067142 (19/12/2014) - P189.0 WO) – COMPOSITION AND METHOD FOR WOOD OR DERIVATIVES OF WOOD.
Authors: Crista, D.M.A, Esteves da Silva, J.C.G.; Mendonça, C..
Entity: Universidade do Porto.

2.3.6 Conclusions

Carbon dots were successfully applied as optical fluorescence sensors for the detection and quantification of reactive oxygen species and carbohydrates.

Upconversion nanoparticles based on lanthanide ions were synthesized and used for nanothermometry and security applications.

The carbon footprint of a cork board (ICB) was evaluated through a life cycle analysis. It has been shown to have a negative footprint due to the use of cork, a renewable raw material. Comparison with other commercial products showed the superiority of ICBs from a carbon footprint point of view.

Novel phosphorescent and iridescent coatings were developed for wood products, toward electricity-free illumination purposes.

Hollow nanostructured microspheres were prepared and tested in the release of model molecules. After the successful optimization of hollow nanostructured, the photocatalysis studies will be performed.

Doped titanium dioxide nanoparticles were synthesized and successfully employed as photocatalysts for the photodegradation of pollutants.

For the first time, DES were used with the purpose of mesoporosity development in silica nano and micromaterials.

Nano Fe_3O_4@ MCM-41 materials were successfully prepared to load and control release of antioxidants molecules. Caffeic acid upload and release was used as model for antioxidant controlled release.

The toxicity of lab synthesized stable and biocompatible mesoporous silica-coated ferromagnetic nanoparticles to release caffeic acid (CA/Fe3O4@ MCM-41) was tested toward aquatic species. The results obtained clearly showed that consistent changes in toxicity of the nano Fe_3O_4@ MCM-41 can be expected after its capping with CA and stabilization with PVA. PVA showed a clear contribution in reducing the toxic effect mainly in case of *V. fischeri* acute toxicity test.

Very sensitive functional surfaces were prepared by electrochemical polymerization of pyrrole (p-Py) on gold screen-printed electrode. The functional surfaces were used with success in the determination of ovary cancer biomarkers (e.g. CA-125).

Sensitive and selective surfaces were prepared by electrochemical polymerization of Toluidine Blue on gold screen-printed electrode. The surfaces were successfully used for the determination of CA 15-3 protein in spiked serum samples with satisfactory results

Single-molecule photosensitizers capable of intracellular self-activation and tumor-selectivity (due to a chemiluminescent reaction with a cancer markers) were developed for the first time. These molecules generate single oxygen, without requiring a light source or any catalyst/co-

factor. Cytotoxicity assays show that these novel molecules induce significant toxicity toward tumor cells, even better than reference drugs, while not inducing toxicity toward normal cells. Such photosensitizers eliminate the current restrictions that photodynamic therapy of cancer presents regarding tumor size and localization.

A set of spectroscopic and theoretical techniques were developed to successfully elucidate the chemiexcitation mechanism of chemiluminescent systems, namely the class of marine imidazopyrazinones. The kinetic and energy profiles of the chemiluminescent reactions were obtained in pH solutions, allowing to determine a pronounced effect of the pH on the resulting light emission.

2.4 Research Task: 4 - MENERG - Materials for Energy Production, Storage and Transport

Responsible Scientist: Prof Doutor Luís Manuel Neves Belchior Faia dos Santos

Goals:
Research and development activities targeting the improvement of the efficient and sustainable energy production, transport and storage including semiconductors synthesized by organic matter, bio-fuels, and developing transport materials and devices.
This task was centred in: the study of thermodynamics properties of biofuels and their pollutant components; the development of new protic ionic liquids for biomass processing; exploring new organic semiconductors for energy applications; the use and development of thin film of ionic liquids in graphene for electronic and energy applications.

2.4.1. Description of activities and results

1. The thermodynamic properties of several aromatic compounds were intensively studied. These chemical compounds comprise environment pollutants that are often present in complex biofuel mixtures. The experimental studies comprised determinations of the energy of combustion using bomb calorimetry and the evaluation of their volatility through vapour pressure measurements at different temperatures. Quantum chemical calculations and empirical correlations were used to develop methods aiming the estimation of those thermodynamic properties and the establishment of relationships between molecular structure and energy.

2. The dispersion and functionalization of graphene and carbon nanotubes in liquid phase has been investigated with a toolbox of imaging and spectroscopic methods and using amphiphilic molecules (surfactants and polymers) as noncovalent dispersants. A rigorous control of the dispersion conditions and accurate definition of quantitative parameters has provided relations between the amphiphile molecular properties and their dispersing efficiency and allowed to understand both equilibrium ansd kinetic aspects of the dispersion process. These studies provided also the basis for the build-up of hybrid CNT-graphene 3D materials via noncovalent interactions, aiming ultimately at electrocatalytic applications in fuel cells.

3. New estimation equations of several properties related with the environmental mobility of pollutant compounds were derived and published in a prestigious journal.

4. Achievements on the development of high purity and crystalline thin films of perovskites and organic hole transporting materials by a vapor deposition. Advances in the study of optical, thermodynamic and morphological properties of naphthyl-substituted benzidines and other organic semiconductor materials.

5. Description of the last developments concerning the state of the Art Knudsen effusion methodology for vapor pressure measurements of low volatile liquids and solids based on a quartz crystal microbalance.
Important review and relevant physical-chemistry properties of energetic materials series as n-Alkanes and their Monosubstituted Derivatives.

6. Development of a model for the nucleation and growth of microdroplets of ionic liquids deposited by physical vapor method.

Advances in the study of ionic liquid based materials and in the support of the nano structuration model of ionic liquids. Achievements in the studies of solid-liquid equilibrium and heat capacity trend in the alkylimidazolium series. Contribution to the understanding of the solvation of alcohols in ionic liquids and the effect of the anion and cation.

Relevant insights on the thermodymamic studies of protic ionic liquids based on the experimental evidence for azeotrope formation from protic ionic liquids.

2.4.2. Deviations from the approved project

For the experimental determination of the fluorescence quantum yield of organic semiconductors, a Quantauros-QY absolute photoluminescence spectrometer was used. Recently we found some anomalies of the results revealing that the apparatus needs to be recalibrated in order to obtain reliable results. This will be done in a technical department of Hamamatsu in Germany.

The intensity of the R&D tasks have been affected by the delay of the project kickoff and specially affected by the limitation of the budged which could be used to support the update and maintenance of the existent equipment.

2.4.3. Scientific Publications

1. Almeida, A.R.R.P.; Pinheiro, B.D.A.; Lima, C.F.R.A.C.; Santos, A.F.L.O.M. ; Ferreira, A.C.S.; Paz, F.A.A. ; Monte, M.J.S. Thermodynamic properties of moldy-musty contaminants of wine. *J. Chem. Eng. Data* **2019**, Accepted: 25.04.2019. https://doi.org/10.1021/acs.jced.9b00062

2. Oliveira, J.A.S.A.; Morais, V.M.F.; Monte, M.J.S. Thermodynamic properties of phase transitions of phenyl derivatives of maleic anhydride and oxazole. *J. Chem. Thermodyn.* **2019**, *131*, pp. 489-494. https://doi.org/10.1016/j.jct.2018.12.001

3. Almeida, A.R.R.P.; Freitas, V.L.S.; Campos, J.I.S.; Ribeiro da Silva, M.D.M.C.; Monte, M.J.S. Volatility and thermodynamic stability of vanillin. *J. Chem. Thermodyn.* **2019**, *128*, pp. 45-54. https://doi.org/10.1016/j.jct.2018.07.023

4. Almeida, A.R.R.P.; Notario, R.; Monte, M.J.S. Vapour pressures and thermodynamic stability of the three aminophenol isomers. *J. Chem. Thermodyn.* **2019**, *129*, pp. 130–137. https://doi.org/10.1016/j.jct.2018.09.011

5. Silva, Ana L.R.; Moura, C.; Ribeiro da Silva, M.D.M.C. Energetic vs structural study of two biomass degradation derivatives: 2-cyclopentenone and 3-methyl-2-cyclopentenone. *J. Chem. Thermodyn.* **2019**, *132*, pp. 390-396. https://doi.org/10.1016/j.jct.2019.01.012

6. Freitas, V.L.S.; Ribeiro da Silva, M.D.M.C. Thermodynamic properties of ε-caprolactam and ε-caprothiolactam. *J. Chem Thermodyn.* **2019**, *132*, pp. 451-460. http://dx.doi.org/10.1016/j.jct.2019.01.014

7. Ledo, J.M.; Flores, H.; Freitas, V.L.S.; Solano-Altamirano, J.M.; Hernández-Pérez, J.M.; Ribeiro da Silva, M.D.M.C.; Camarillo, E.A. Thermal and structural properties of ethyl 2- and 3-aminobenzoates: experimental and computational approaches. *J. Chem Thermodyn.* **2019**,

133, pp. 93-99. http://dx.doi.org /10.1016/j.jct.2019.02.001

8. Abreu, B.; Rocha, J.; Fernandes, R.M.F.; Regev, O.; Furó, I.; Marques, E.F. Gemini surfactants as efficient dispersants of multiwalled carbon nanotubes: Interplay of molecular parameters on nanotube dispersibility and debundling. *J. Colloid Interface Sci.* **2019**, *547*, pp. 69–77. https://doi.org/10.1016/j.jcis.2019.03.082

9. Lobo Ferreira, A.I.M.C.; Rodrigues, A.S.M.C.; Villas, M.; Tojo, E.; Rebelo, L.P.N.; Santos, L.M.N.B.F. Crystallization and Glass-Forming Ability of Ionic Liquids: Novel Insights into Their Thermal Behavior. *ACS Sustainable Chemistry & Engineering* **2019**, *7*, pp. 2989–2997. https://doi.org/10.1021/acssuschemeng.8b04343

10. Costa, J.C.S.; Santos, L.M.N.B.F. Chain-Length Dependence of the Thermodynamic Behavior of Homologous α,ω-Disubstituted Alkanes. *Journal of Chemical and Engineering Data* **2019**, *64*, pp. 2229–2246. https://doi.org/10.1021/acs.jced.9b00125

11. Dávalos, J.Z.; Lima, C.F.R.A.C.; Santos, L.M.N.B.F.; Romero, V.L.; Liebman, J.F. Thermochemical and structural studies of gallic and ellagic acids. *The Journal of Chemical Thermodynamics* **2019**, *129*, pp. 108–113. https://doi.org/10.1016/j.jct.2018.09.027

12. Pokorný, V.; Serra, P.B.P.; Fulem, M.; Lima, C.F.R.A.C.; Santos, L.M.N.B.F.; Růžička, K. Heat Capacity and Phase Behavior of Selected Oligo(ethylene glycol)s. *Journal of Chemical and Engineering Data* **2019**, *64*, pp. 2742–2749. https://doi.org/10.1021/acs.jced.9b00140

13. Rodrigues, A.S.M.C.; Fernandes, A.M.; Dévemy, J.; Costa Gomes, M.; Santos, L.M.N.B.F. Fluorination effect in the volatility of imidazolium-based ionic liquids. *Journal of Molecular Liquids* **2019**, *282*, pp. 385–391. https://doi.org/10.1016/j.molliq.2019.03.024

14. T. E. Sintra, Vilas, M.; Martins, M.; Ventura, S.P.M.; Lobo Ferreira, A.I.M.C.; Santos, L.M.N.B.F.; Gonçalves, F.J.M.; Tojo, E.; Coutinho, J.A.P. Synthesis and Characterization of Surface-Active Ionic Liquids Used in the Disruption of Escherichia Coli Cells. *ChemPhysChem* **2019**, *20*, pp. 727–735. https://doi.org/10.1002/cphc.201801127

15. Nadiv, R.; Fernandes, R.M.F.; Ochbaum, G.; Dai, J.; Buzaglo, M.; Varenik, M.; Biton, R.; Furó, I.; Regev, O. Polymer nanocomposites: Insights on rheology, percolation and molecular Mobility. *Polymer* **2018**, *153*, pp. 52–60. https://doi.org/10.1016/j.polymer.2018.07.079

16. Dai, J.; Fernandes, R.M.F.; Regev, O.; Marques, E.F.; Furó, I. Dispersing Carbon Nanotubes in Water with Amphiphiles: Dispersant Adsorption, Kinetics, and Bundle Size Distribution as Defining Factors. *J. Phys. Chem. C* **2018**, *122*, pp. 24386−24393. http://dx.doi.org/10.1021/acs.jpcc.8b06542

17. Fernandes, R.M.F.; Dai, J.; Regev, O.; Marques, E.F.; Furó, I. Block Copolymers as Dispersants for Single-Walled Carbon Nanotubes: Modes of Surface Attachment and Role of Block Polydispersity. *Langmuir* **2018**, *34*, pp. 13672−13679. http://dx.doi.org/10.1021/acs.langmuir.8b02658.

18. Silva, A.L.R.; Matos, M.A.R.; Morais, V.M.F.; Ribeiro da Silva, M.D.M.C. Thermochemical and conformational study of optical active phenylbenzazole derivatives. *J. Chem.Thermodyn.* **2018**, *116*, pp. 7–20. http://dx.doi.org/10.1016/j.jct.2017.08.017

19. Freitas, V.L.S.; P.J.O. Ferreira, Ribeiro da Silva, M.D.M.C. Experimental and computational thermochemical studies of acridone and N- methylacridone. *J. Chem.*

Thermodyn. **2018**, *118*, pp. 115–126. http://dx.doi.org/10.1016/j.jct.2017.11.002

20. Silva, A.L.R.; Gonçalves, J.M.; Ribeiro da Silva, M.D.M.C. Experimental and computational thermochemical study of two fluorobenzazoles: 5- fluoro-2-methylbenzoxazole and 5-fluoro-2-methylbenzothiazole. *J. Chem. Thermodyn.* **2018**, *120*, pp. 157-163. http://doi.org/10.1016/j.jct.2018.01.022

21. Dávalos, J.Z.; Valderrama-Negrón, A.C.; Barrios, J.; Freitas, V.L.S.; Ribeiro da Silva, M.D.M.C. Energetic and structural properties of two phenolic antioxidants: tyrosol and hydroxytyrosol. *J. Phys. Chem. A* **2018**, *122*, pp. 4130–4137. http://dx.doi.org/10.1021/acs.jpca.8b00457

22. Monte, M.J.S.; Almeida, A.R.R.P.; Notario, R. Volatility and chemical stability of chromium, molybdenum, and tungsten hexacarbonyls. *J. Thermal Anal. Calorim*. **2018**, *132*, pp. 1201–1211. https://doi.org/10.1007/s10973-018-7033-1T4-4

23. Silva, A.L.R.; Morais, V.M.F.; Ribeiro da Silva, M.D.M.C. Thermodynamic properties of naphthoxazole and naphthothiazole derivatives: experimental and computational studies. *J. Chem. Thermodyn.* **2018**, *127*, pp. 45-55. https://doi.org/10.1016/j.jct.2018.07.008

24. Silva, A.L.R.; Lima, A.C.M.O.; Ribeiro da Silva, M.D.M.C. Energetic characterization of indanone derivatives involved in biomass degradation. *J. Thermal Anal. Calorim.* **2018**, *134*, pp. 1267–1276. https://doi.org/10.1007/s10973-018-7533-z

25. Perdomo, G.; Ramos, F.; Notario, R.; Freitas, V.L.S.; Ribeiro da Silva, M.D.M.C.; Camarillo, E.A.; Dávalos, J.Z. Thermochemistry of R-SH group in gaseous phase: experimental and theoretical studies of three sulfur imidazole derivatives. *J. Chem. Thermodyn.* **2018**, *122*, pp. 65–72. http://dx.doi.org /10.1016/j.jct.2018.03.002

26. Freitas, V.L.S.; Silva, C.A.O.; Ribeiro da Silva, M.D.M.C. Energetic vs structural effects of aminoalkyl substituents in the morpholine. *J. Chem. Thermodyn.* **2018**, *122*, pp. 95–101. http://dx.doi.org/10.1016/j.jct.2018.03.001

27. Costa, J.C.S.; Azevedo, J.; Araújo, J.P.; Santos, L.M.N.B.F.; Mendes, A. High purity and crystalline thin films of methylammonium lead iodide perovskites by a vapor deposition approach. *Thin Solid Films* **2018**, *664*, pp. 12–18. https://doi.org/10.1016/j.tsf.2018.08.026

28. Santos, L.M.N.B.F.; Lobo Ferreira, A.I.M.C.; Stejfa, V.; Rodrigues, A.S.M.C.; Rocha, M.A.A.; Torres, M.C.; Tavares, F.M.S.; Carpinteiro, F.S. Development of the Knudsen effusion methodology for vapour pressure measurements of low volatile liquids and solids based on a quartz crystal microbalance. *J. Chem. Thermodyn.* **2018**, *126*, pp. 171–186. https://doi.org/10.1016/j.jct.2018.07.004

29. Costa, J.C.S.; Mendes, A.; Santos, L.M.N.B.F. Thin-film Deposition of Organic Hole Transporting Materials: Optical, Thermodynamic and Morphological Properties of Naphthyl-Substituted Benzidines. *Journal of Materials Science* **2018**, *53*, pp. 12974–12987. https://doi.org/10.1002/cphc.201800335

30. Ribeiro, F.M.S.; Lima, C.F.R.A.C.; Silva, A.M.S.; Santos, L.M.N.B.F. Experimental Evidence for Azeotrope Formation from Protic Ionic Liquids. *ChemPhysChem* **2018**, *19*, pp. 2364–2369. https://doi.org/10.1002/cphc.201800335

31. Costa, J.C.S.; Coelho, A.F.S.M.G.; Mendes, A.; Santos, L.M.N.B.F. Nucleation and Growth of Microdroplets of Ionic Liquids Deposited by Physical Vapor Method onto Different Surfaces. *Applied Surface Science* **2018**, *428*, pp. 242–249. http://dx.doi.org/10.1016/j.apsusc.2017.09.137

32. Costa, J.C.S.; Mendes, A.; Santos, L.M.N.B.F. Chain Length Dependence of the Thermodynamic Properties of n-Alkanes and their Monosubstituted Derivatives. *J. Chem. Eng. Data* **2018**, *63*, pp. 1–20. http://dx.doi.org/10.1021/acs.jced.7b00837

33. Serra, P.B.P.; Ribeiro, F.M.S.; Rocha, M.A.A.; Fulem, M.; Růžička, K.; Coutinho, J.A.P.; Santos, L.M.N.B.F. Solid-Liquid Equilibrium and Heat Capacity Trend in the Alkylimidazolium PF6 Series. *Journal of Molecular Liquids* **2017**, *248*, pp. 678–687. http://dx.doi.org/10.1016/j.molliq.2017.10.042

34. Freitas, V.L.S.; Gomes, J.R.B.; Ribeiro da Silva, M.D.M.C. Thermochemical studies on two alkyl-bulky substituted xanthene derivatives: 9,9- dimethylxanthene and 2,7-di-tert-butyl-9,9-dimethylxanthene. *J. Chem. Thermodyn.* **2017**, *106*, pp. 168–177. http://dx.doi.org/10.1016/j.jct.2016.11.020

35. Almeida, A.R.R.P.; Monte, M.J.S. Vapour pressures and phase transition properties of four substituted acetophenones. *J. Chem. Thermodyn.* **2017**, *107*, pp. 42–50. https://doi.org/10.1016/j.jct.2016.12.012

36. Oliveira, J.A.S.A.; Notario, R.; Ribeiro da Silva, M.D.M.C.; Monte, M.J.S. Vapour pressures, enthalpies, and Gibbs energies of formation and sublimation of fluorene-2-carboxaldehyde. *J. Chem. Thermodyn.* **2017**, *111*, pp. 65–71. http://dx.doi.org/10.1016/j.jct.2017.03.021

37. Silva, A.L.R.; Ribeiro da Silva, M.D.M.C. Comprehensive thermochemical study of cyclic five and six-membered N,N´-thioureas. *J. Chem. Eng. Data* 62, pp. 2584–2591. http://pubs.acs.org/doi/pdf/10.1021/acs.jced.7b00083

38. Silva, A.L.R.; Ribeiro da Silva, M.D.M.C. Energetic, structural and tautomeric analysis of 2-mercapto-benzimidazole: an experimental and computational approach. *J. Thermal Anal. Calorim.* **2017**, *129*, pp. 1679–1688 https://link.springer.com/article/10.1007%2Fs10973-017-6353-x

39. Freitas, V.L.S.; Silva, C.A.O.; Paiva, M.A.T.; Ribeiro da Silva, M.D.M.C. Energetic effects of alkyl groups (methyl and ethyl) on the nitrogen of the morpholine structure. *J. Thermal Anal. Calorim.* **2017**, *130*, pp. 485–496. http://dx.doi.org/10.1007/s10973-017-6194-7

40. Almeida, A.R.R.P.; Monte, M.J.S. Estimations of the thermodynamic properties of halogenated benzenes as they relate to their environment mobility. *Chemosphere* **2017**, *189*, pp. 590–598. https://doi.org/10.1016/j.chemosphere.2017.09.095

41. Freitas, V.L.S.; Gomes, J.R.B.; Liebman, J.F.; Ribeiro da Silva, M.D.M.C. Energetic and reactivity properties of 9,10-dihydroacridine and diphenylamine: a comparative overview. *J. Chem. Thermodyn.* **2017**, *115*, pp. 276–284. http://dx.doi.org/10.1016/j.jct.2017.08.001

2.4.4. PhD Thesis

Concluded

1. Filipe Miguel da Silva Ribeiro, Protic Ionic Liquids for Biomass Processing.
   PhD. Thesis In Sustainable Chemistry. Faculdade de Ciências da Universidade do Porto 2018, UP, Portugal

2. Ana Sofia Moreira Conde Rodrigues, Isomerization Effect on the Physical-chemical properties of ionic liquids and polyphenyls.
   PhD. Thesis in Chemistry, Faculdade de Ciências da Universidade do Porto 2017, UP, Portugal

3. Nuno Filipe Martins Branco, Estudo de propriedades de sistemas Gasóleo/Fame numa perspectiva de identificação de causas e mecanismos relacionadas com "envelhecimento químico" e alteração de características de frio.
   PhD. Thesis in Refining, Petrochemical and Chemical Engineering
   Universidade de Aveiro & Faculdade de Ciências da Universidade do 2019, UP/UA, Portugal

In progress:

1. Carlos Alexandre Oliveira da Silva, Determinação e estabelecimento de modelos de previsão de propriedades termodinâmicas de fragrâncias químicas: Ferramentas para a avaliação de riscos ambientais
   PhD. Thesis in Chemistry, Faculdade de Ciências da Universidade do Porto Início: 1 de Outubro 2018, UP, Portugal

2. Inês Catarina Moreira Vaz, Ionic Liquids for the Sustainable Solvent Design and Functional Materials Application
   PhD. Thesis in Chemistry, Faculdade de Ciências da Universidade do Porto
   Início: 1 de Marco 2016, UP, Portugal

3. Bárbara Catarina Abreu Teixeira, Building doped graphene/carbon nanotube hierarchical assemblies via surfactant-mediated interactions for advanced applications,
   PhD. Thesis in Chemistry, Faculdade de Ciências da Universidade do Porto
   Início: 1 de setembro 2016, UP, Portugal.
   Supervisor: E.F. Marques. Co-supervisor: C. Freire.

2.4.5. Patents

No Patents in this period

2.4.6 Conclusions

Contribution to the development of the knudsen effusion methodology for vapour pressure measurements of low volatile liquids and solids based on a quartz crystal microbalance.

High accuracy energies of combustion and thermodynamic properties related to the volatility of several biofuel components were successful determined.

Relationships between structural energetic properties were established aiming at the prediction of the reactivity of those chemical compounds.

Environmental mobility properties of several pollutant components were determined; a new and simple method of estimation some of these properties was settled.

Successful measurement and interpretation of the heat capacity and phase behavior of oligo(ethylene glycol)s.

Fabrication of high purity and crystalline thin films of methylammonium lead iodide perovskites by a vapor deposition approach.

Successful thin-film deposition of organic hole transporting materials and measurement of optical, thermodynamic and morphological properties.

Development of a nucleation and growth of microdroplets of ionic liquids deposited by physical vapor method.

Novel Insights into the thermal behavior of ionic liquids: Solid-liquid equilibria; glass transition and glass forming behavior; heat capacity correlations of ionic liquid series.

Relevant contribution to the interpretation of the nanostructuration of ionic liquids and ionic liquid mixtures. Fluorination effect in the volatility of ionic liquids and the formation/appearance of a new apolar fluorinate domain.

The use of gemini surfactants as efficient dispersants of multiwalled carbon nanotubes. Molecular insights on kinetic and equilibrium aspects of the dispersion of carbon nanotubes and graphene by amphiphiles (surfactants and polymers). Progress on the characterization of studied polymer nanocomposites: insights on rheology, percolation and molecular mobility.