Universidade do Minho

CENTRE OF CHEMISTRY

UNIVERSITY OF MINHO

REPORT

2018-2023

The present report concerns to the period from 1st January 2018 to 31st December 2023, financed by the Fundação para a Ciência e Tecnologia (FCT Portugal) through funding UID/QUI/00686/2016, UID/QUI/00686/2019, and from Base funding UIDB/00686/2020 and Programmatic funding UIDP/00686/2020.

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1. Organization and governance

The Centre of Chemistry of University of Minho (CQUM) is organized into 3 research groups, Applied Biomolecular Chemistry (ABC), Heterocycles for Societal Challenges (HSC) and Sustainable Chemistry - New Methods and Materials (SC). Each group includes members aligned with common interests that support the mission of conducting high-quality scientific research. All researchers are members of the Scientific Council of CQUM, which every three years elects the Director. Each research group has one coordinator, assisted by an elected representative of the group members.

1.1. Board

Maria Manuela Silva (Director, coordinator SC)

Maria Alice Carvalho (Deputy Director, representative HSC)

Maria Fernanda Proença (coordinator HSC)

Luís Monteiro (coordinator ABC)

Susana Costa (representative ABC)

Rui Pereira (representative SC)

1.2. External advisory board

Prof. Bing Xu (Department of Chemistry, Brandeis University, USA)

Prof. Nuno Maulide (Institute of Organic Chemistry, University of Viena, Austria)

Prof. Miguel Bañares (CSIC - Instituto de Catálisis y Petroleoquímica, Madrid, Spain)

2. Strategic aims

CQUM promotes research and advanced training in the field of chemistry at the interface with biology, physics, materials science, medicine and nanoscience, within two interdisciplinary thematic areas, Synthetic Chemistry and Functional Materials. The main goals are the use of biomolecules as targets and/or tools for application in drug delivery, medical diagnostics and bioimaging, the preparation and characterization of new drug candidates for unmet clinical needs, the preparation and modification of new materials for future technological solutions,

and the development of analytical techniques for pollutants control. The CQUM also has a significant role in the creation and transfer of knowledge through development of R&D projects with external entities.

2.1 Research highlights

1. New bioactive compounds for diseases such as microbial infections by multi-resistant pathogens, cancer, diabetes or Alzheimer's.
2. Application of (bio)molecules in medical diagnosis and bioimaging probes.
3. Nanomaterials for controlled delivery of drugs.
4. New adaptable, smart and sustainable materials for various technological applications, such as batteries (cathodes, anodes, separators, electrolytes), electrochromic devices, sensors and biomaterials.
5. Analytical devices and methodologies for environmental monitoring and waste recovery.

3. Research unit description

The CQUM is a research unit financed by the Foundation for Science and Technology, being an organic subunit of the School of Sciences of the University of Minho. Between 2018-2023 the number of integrated members[1] varied between 31 and 28 (in 2023, 22 academics and 6 researchers) (**Figure 1**).

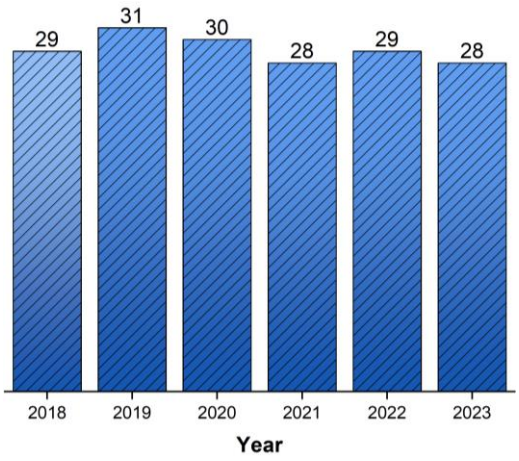

Figure 1. Number of integrated researchers in 2018-2023.

[1] Integrated PhD holder researcher: PhD holder researcher with a contract or link with a Portuguese institution and who dedicates working time to research activities in an R&D Unit.

During 2018-2023, the research at CQUM focused on synthetic chemistry and the preparation and characterization of functional materials, through the interaction between three research groups, Applied Biomolecular Chemistry (ABC), Heterocycles for Societal Challenges (HSC) and Sustainable Chemistry - New Methods and Materials (SC), and collaborations with UMinho's R&D units, other national and international research units and external entities.

The research includes the discovery and development of new bioactive compounds for unmet clinical needs such as selective therapeutic systems for various diseases (e.g. microbial infections, cancer, diabetes or Alzheimer's), the development of nanomaterials for the controlled transport and release of drugs, the application of (bio)molecules in medical diagnosis, probes for bioimaging, the extraction and encapsulation of natural products for application as biopesticides and food preservatives, the development of new functional, smart and sustainable materials for a wide range of applications including biomedical use, optoelectronics, energy storage, catalysts, smart windows and sensors, the development of green synthetic methodologies based on by-products, analytical methodologies aimed at environmental monitoring and waste recovery. The research developed by the 28 integrated members (**Table 1**) in the three research groups is summarized below.

ABC researchers are involved **1**) in the design, synthesis, characterization and *in vitro* and *in vivo* evaluation of metal chelates and functionalized nanostructures as contrast agents for medical imaging (MRI, PET, SPECT), **2**) on peptide-based nanoconstructed scaffolds and self-assembled hydrogels as drug delivery and cancer theranostic platforms, **3**) on the computational design and synthesis of unnatural amino acids, peptide analogues and peptidomimetics with antimicrobial, antifungal, and anti-inflammatory activities for lower respiratory tract infections and the functionalization of fibrous materials for the treatment of chronic wounds, **4**) synthesis of heterocyclic phototriggers for controlled drug delivery by one- and two-photon excitation, **5**) synthesis and application of heterocyclic fluorophores for cellular imaging, **6**) application of plant extracts as natural and semisynthetic insecticides, biopesticides and antifungal agents and **7**) study of the effect of several crowding agents and salts in the folding of bovine serum albumin and myoglobin, taken as model proteins for the development of new formulations for the stabilization of biopharmaceuticals.

Researchers of **HSC** have applied their expertise in organic chemistry to two major research topics: synthesis of new heterocycle compounds and new materials. The main goal pursued was the development of new synthetic methods to prepare new heterocycles to be used as

therapeutic drugs or diagnostic tools or used as new materials. It focuses on **1)** the preparation of novel fluorescent analogues of purine nucleobases to study their photophysical properties for the development of new applications as biosensors, **2)** new coating materials with biological properties, **3)** the synthesis of a variety of heterocycles with biological activity against cancer, schizophrenia, leishmaniasis, sleeping sickness, neurodegenerative diseases, malaria, bacteria, and infectious yeasts, **4)** the incorporation of heterocyclic second harmonic generation and photochromic compounds in nanofibers, polymer matrices and liquid crystals, and evaluation of their photophysical, nonlinear optical, photochromic, catalytic and dye-sensitized solar cell properties, and **5)** the computational design of new heteroditopic systems and the study of their chemosensory ability, in solution, as selective fluorimetric and/or colorimetric sensors of ions and molecules with analytical, biological and environmental relevance. The discovery of potent and selective compounds with anticancer, antileishmanial, and antimalarial activity prompted its protection by patents, and a spin-off company (Karion Therapeutics) was created to translate the research in anticancer compounds into the clinic. Collaboration with local industry to solve particular issues was also developed.

The **SC** group developed new functional and eco-sustainable materials for applications in environmental protection, energy, water safety, health and analytical methodologies. The research was developed on the following topics: **1)** polymeric membranes for the removal of pollutants in effluents, **2)** formulation of ecological, chemically stable, low toxicity and non-flammable aqueous paints, **3)** disposable microfluidic methodologies and devices for simultaneous detection of biomarkers in the sputum of patients with lung diseases, **4)** sensors based on optical fibers for monitoring humidity, pH, and chloride, sodium and potassium ions in concrete structures, **5)** thermoreversible hydrogels for selective release of active species in textile applications, **6)** biopolymers as components (electrolytes/separators, cathodes and anodes) for sustainable electrochemical devices, namely lithium batteries and electrochromic devices (smart windows) and production of super-hydrophobic films inspired by nature, **7)** use of carbon nanomaterials and metals for the development of sensors based on highly selective recognition elements (affinity interaction) for the detection of toxins and allergens and the quantification of pollutants in effluents and the organic fraction of municipal solid waste (compound) for the treatment of wastewater and diffuse pollution, **8)** Treatment of effluents and recovery of biomass using nanomaterials (zeolites and carbon) by catalytic and

electrochemical methods, and **9)** use of zeolites in the development of drug and antimicrobial delivery systems.

Table 1. Integrated members of CQUM by the end of 2023.

Name	Category*	Group	ORCID ID	SCOPUS ID
Alice Maria Esteves Dias	Assis. Prof.	HSC	0002-5111-0774	35497113600
Ana Paula A. Faria Bettencourt Estevão	Assis. Prof.	SC	0002-6523-1219	6603687675
Ana Paula da Assunção Esteves	Assoc. Prof.	HSC	0002-7837-5983	7006412185
António Belmiro Gil Silva Fortes	Assis. Prof.	HSC	0002-8754-2472	7004475753
António Maurício da Costa Fonseca	Assoc. Prof. Hab	SC	0001-9624-7208	26029442800
Daniela Maria Silva Correia	Jun. Res.	SC	0002-3118-4717	54413981400
Filipe Carlos Teixeira Gil	Assis. Res.	HSC	0001-8786-0086	10038915500
João Carlos Ramos Nunes Marcos	Assis. Prof.	ABC	0001-5529-9597	57203855899
João Paulo Rodrigues André	Assis. Prof.	ABC	0001-6761-171X	7401495971
José Alberto Ribeiro Martins	Assis. Prof.	ABC	0001-9323-3978	36184713800
Luís Miguel Oliveira Sieuve Monteiro	Assoc. Prof.	ABC	0001-7779-9250	7103010477
Maria Alice Gonçalves Carvalho	Assis. Prof.	HSC	0002-8666-0362	16644798200
Maria de Fátima Malveiro Bento	Assis. Prof.	SC	0003-0106-2089	57193088122
Maria do Sameiro Torres Gonçalves	Assis. Prof.	ABC	0003-2048-1190	7202320514
Maria Dulce da Silva Geraldo	Assis. Prof.	SC	0002-2415-6056	6603188447
Maria Fernanda Jesus Rego Paiva Proença	Full Prof.	HSC	0002-5274-1949	12139711000
Maria Gabriela Coutinho Botelho	Assis. Prof.	SC	0002-4680-0834	6701608285
Maria Isabel Pontes Correia Neves	Assoc. Prof. Hab	SC	0001-9705-9444	57196690183
Maria João Ribeiro Peixoto Queiroz	Coord. Res.	HSC	0002-4322-8035	7102888796
Maria Manuela da Silva Pires Silva	Assoc. Prof. Hab	SC	0002-5230-639X	57054186900
Maria Manuela Marques Raposo	Assoc. Prof. Hab	HSC	0002-7996-1626	7005684062
Paula Margarida V. S. Teixeira Ferreira	Assoc. Prof.	ABC	0002-3279-6731	55947741900
Pier Parpot	Assoc. Prof.	SC	0002-3918-2839	6603358868
Renato Ferreira Gonçalves	Jun. Res.	SC	0001-9763-7371	37009149800
Rui Francisco G. P. Fernandes Pereira	Jun. Res.	SC	0001-7279-5728	14033257200
Sandra Maria P. Cerqueira	Jun. Res.	SC	0002-4001-2896	7006913220
Sílvia Manuela M. Alves Pereira Lima	Assis. Prof.	ABC	0003-4310-8292	8948810400
Susana Paula Graça Costa	Assis. Prof.	ABC	0001-7915-4720	7201998849

* Assis. Prof.: Assistant Professor; Assoc. Prof.: Associate Professor; Full Prof.: Full Professor; Hab: with Habilitation; Coord. Res.: Coordinator Researcher; Jun. Res.: Junior Researcher; Assis. Res.: Assistant Researcher.

Regarding advanced training, between 2018 and 2023, there was a sustained increase in the number of doctoral students supervised/co-supervised by integrated members of CQUM, as can be seen in **Table 2**. The completion of the theses was affected by the Covid-19 pandemic, which significantly impacted the progress of the research work due to the complete closure of

facilities. It is expected that in a near future a significant number of PhD students will finish their works. Also, there is a considerable number of master students (98 students in 2023) supervised/co-supervised by members of CQUM.

Table 2. Evolution of the number of PhD students in the period 2018-2023.

	Year					
	2018	**2019**	**2020**	**2021**	**2022**	**2023**
On going (new grants)	24 (2)	27 (6)	34 (7)	37 (9)	40 (6)	40 (7)
Finished	3	1	2	3	6	6

3.1 Infrastructure

CQUM is installed at the main building of School of Sciences occupying a total area of *ca*. 2500 m^2, including wet and dry laboratories which have basic equipment to perform all the daily experimental activities. Larger equipment for the characterization of new molecules and materials (NMR, UV-vis absorption, fluorimeter, elementary analyser, FTIR-ATR, DSC, HPLC, GC and LC-MS) is available to all researchers as common equipment (**Figure 2**).

Spectrofluorometer
Fluoromax 4, Horiba Jobin-Yvon

FTIR-ATR Spectrometer
Spectrum Two, PerkinElmer

LXQ Linear Ion Trap Mass Spectrometer
Thermo Scientific

400 MHz NMR Spectrometer
Avance III, Bruker

Figure 2. Some of the equipment available at CQUM.

More advanced equipment is also available through national collaborative networks, in which CQUM is a partner:

Quanta Lab - the Quanta Lab allows members to work in the preparation of new 2D quantum materials to explore the emergent properties of their new materials.

PT-OPENSCREEN - this network bridges chemistry-based research areas and molecular and structural biology. This is a state-of-the-art infrastructure for basic and applied drug discovery, chemical biology, and genetics research. This platform allows CQUM members access to state-of-the-art technology (cellular and biochemical assays for screening, as well as hit-to-lead, lead optimization, and follow-up studies) to boost their drug discovery and development projects. Additionally, CQUM members contribute with their in-house designed and synthesized compounds to build the national library of Portuguese chemical compounds.

PTNMR – the nuclear magnetic resonance national network provides access to modern and up-to-date NMR spectrometers, offering fundamental analytical services in structural analysis to researchers and industry, stimulating the use of advanced facilities and the sharing of the national scientific resources.

CryoEM-PT - this national network, with a state-of art 200 kV cryo-electron microscope for single particle analysis, cryo-tomography and microcrystal diffraction, allows CQUM members to deepen their knowledge of the interaction of their synthesized molecules with biological targets, contributing to the progress of drug development projects.

4. Publications in 2018-2023 by integrated researchers

For the period 2018-2023, the publications authored by integrated researchers is presented in **Table 3**. The evolution of productivity per integrated member and the impact of the research developed within the unit is presented in **Table 3** and **Figures 3**-**6**. A positive and sustainable evolution is observed in both parameters, as well as in terms of patents.

Table 3 - Number and type of publications in the period 2018-2023.

	Year					
	2018	**2019**	**2020**	**2021**	**2022**	**2023**
Integrated researchers	29	31	30	28	29	28
Articles	43	60	51	64	58	76
Articles Q1 (%)	37 (86)	50 (83)	40 (78)	57 (89)	54 (93)	67 (88)
Articles Q2 (%)	6 (14)	7 (12)	11 (22)	6 (9)	4 (7)	6 (8)
Articles Q3 & Q4 (%)	0	3 (5)	0	1 (2)	0	3 (4)
IF average	3.32	3.83	4.42	5.26	5.78	7.12
Articles/researcher	1.48	1.94	1.70	2.29	2.00	2.71
Patents submitted/published*	1 (NP) 1 (IP)	2 (NP)	3 (IP)	3 (IP)	2 (NP) 1 (IP)	1 (NP) 3 (IP)

* IF – Impact factor; NP – National Patent; IP – International Patent

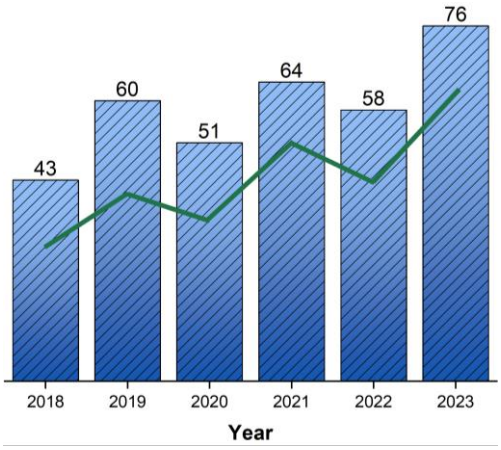

Figure 3. Number of articles per year.

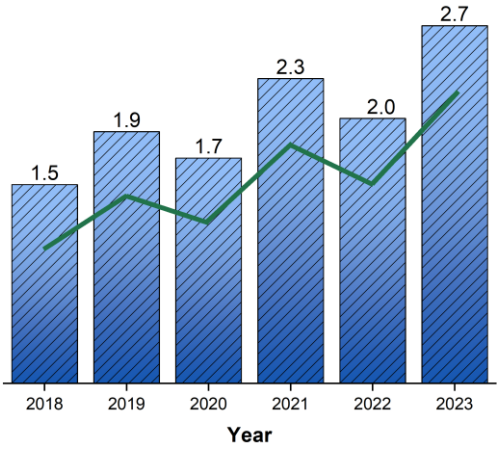

Figure 4. Ratio articles/researcher.

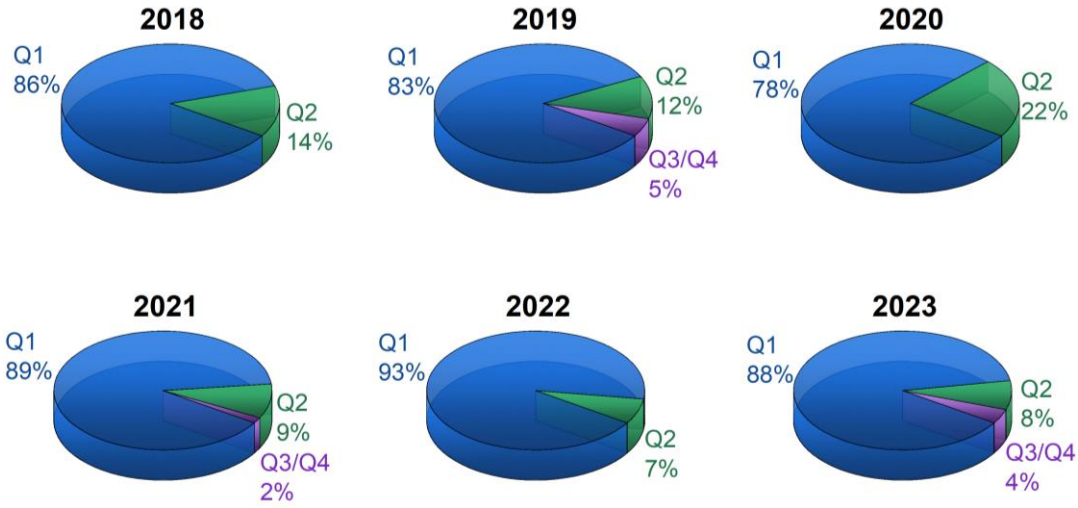

Figure 5. Percentage of publications in quartile Q1, Q2, Q3 and Q4, in the period 2018-2023.

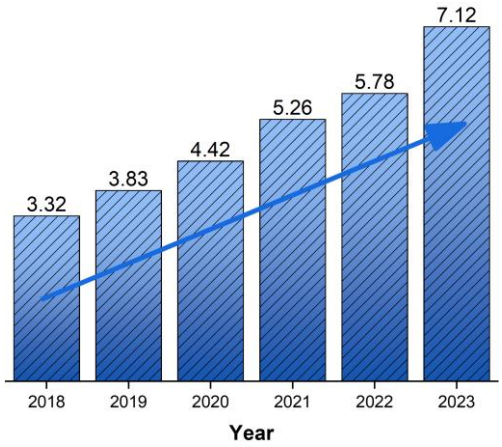

Figure 6. Average IF of articles.

5. Funding in the period 2018-2023

During 2018-2023, the Portuguese agencies, the Foundation for Science and Technology (FCT) and the National Innovation Agency (ANI), continued to be our principal funding sources, although international Projects (INTERREG) and projects funded by the Recovery and Resilience Plan (PRR) represented another very important source of financing. Funding from FCT is divided into two different items. The first corresponds to unit strategic project funding (the unit was classified as good in the last evaluation exercise) and the second to individual research projects. The third item refers to PRR funding. The fourth to other national projects and finally the fifth concerning international funding (**Table 4**).

Table 4. Funding in the period 2018-2023.

	Year					
	2018	**2019**	**2020**	**2021**	**2022**	**2023**
1- Strategic Project FCT (k€)	84.00	54.48	104.95	104.95	104.95	104.95
2- Projects FCT (k€)	325.00	248.30	253.90	148.80	113.70	105.70
3- Projects IAPMEI – PRR (k€)	-	-	-	-	-	71.60
4- Others National Projects (ANI, CCRN) (k€)	45.20	45.20	45.20	25.10	223.30	74 .40
5- International Projects (INTERREG, H2020, ITN, Erasmus and others) (k€)	275.98	142.41	-	-	-	125.00
TOTAL (k€)	730.18	490.39	404.05	278.85	441.95	481.65

6. Dissemination, communication, and exploitation activities

Dissemination and communication activities were developed by all the CQUM members. Dissemination activities to spread a well-defined set of messages, founded in the results of the research performed within the research centre, to a variety of target audiences, through a variety of communication channels (website, posters, talks at international conferences, and high impact peer reviewed journals, such as Chemical Reviews, Advanced Energy Materials, Energy Storage Materials, Chemical Engineering Journal and Carbohydrate Polymers, and conferences such as EuChemS, ECS and ISE meetings) was performed, with a measurable influence on the visibility and impact of the R&D unit.

The Unit has some contact with local, national and international industries demonstrating certain capacity of knowledge transfer to the private sector. Collaboration with companies includes the development of new products or processes. Companies such as Nanopaint for functional inks, Solvay for fluoropolymers binder, Johnson Matthey for active cathode materials, Imerys for anode materials, and Bosch for preparation of electrically conductive hybrid resins are collaborating with members of CQUM and are receptive to testing, leveraging, and implementing the outcomes. Other examples include the development of chitosan nanomaterials for leather protection (NBS Curtumes), the development of a methodology for bleaching oak veneers to improve their commercial value (Fibromade), the development of

protocols for cardanol purification and a sustainable method to generate phenolalkylamines (Resibras) for industrial applications.

7. Internationalization

Researchers at CQUM engage in a substantial number of active international collaborations with European and non-European institutions/companies/universities. The outcome of these international collaborations is clearly reflected in the significant number of Scopus publications with international co-authors (54% of the publications in 2023 are with international collaborations). The international recognition of the quality of research conducted at CQUM was also evidenced in the participation of some researchers as evaluators for international projects from various entities, including the European Commission, and the involvement of researchers as editors/members of editorial boards of several Scopus-indexed journals.

Furthermore, the international recognition of the quality of research conducted at CQUM was also demonstrated through the recent organization or participation in the organization of various international conferences, such as the International Materials Symposium/Congress of the Portuguese Materials Society, the Luso-Galician Chemistry Meeting, the International Electronic Conference on Synthetic Organic Chemistry, the International Symposium on Synthesis and Catalysis, and EuChemS Chemistry Congress, as well as invitations to deliver lectures at international conferences.

8. Final remarks

The activity of CQUM in 2020 and 2021 was disturbed by the atypical situation experienced in the context of the Covid-19 pandemic, which affected the course of the research work with the total closing of the facilities, due to the general confinement decreed by the government, as well as due to the restrictions imposed on the maximum capacity of laboratory spaces and the rotation regime adopted between the researchers, in order to ensure compliance with the distancing rules imposed by the General Directorate of Health.

Considering the above, the planned tasks suffered a delay, since the real impact of the pandemic restrictive measures largely exceeded the actual closing time frame as the restrictions caused delays with cumulative impact. Despite the disturbance, the indicator of productivity in the form of publications maintained a high level and the objectives were achieved. The pursued objectives of the research were of interest and with a positive social and economic impact. The objectives of the plan of activities for 2018-2023 were coherent with the expertise and trajectory of the R&D Unit. The research quality, the national and international relevance, interdisciplinarity and national and international collaboration, were increased during the period 2018-2023. There was considerable integration and coordination between the research within and between the groups at CQUM and synergies among the groups has been demonstrated.

The R&D Unit made significant scientific contributions with an important result in training of Master and PhD Students. The Department of Chemistry (DC) offers 2 master's degrees, namely, Medicinal Chemistry (MQM) and Chemical Analysis and Characterization Techniques (MTCAQ). The Department of Chemistry, in partnership with the Department of Biology, also features a master's in Applied Biochemistry (MBQA). These three master's degrees have been running continuously for *ca*. 15 years with success. Particularly, MTCAQ presents a high demand from students and has intense collaboration with industry and R&D labs. Most of the students develop their MSc thesis under industrial environment leading to the establishment of joint R&D projects involving CQUM researchers. Infrastructure and human resources from CQUM nurture this interaction with industry. The DC also offers a Doctoral Program in Chemistry and a Doctorate in Applied Chemistry, which have seen a steady increase of the number of students in the period in question.

The scientific productivity, in terms of the amount and the quality of the publications, in peer reviewed specialized journals has increased significantly in the last years. The quality of the publications increased by accessing journals of a higher impact factor. Outreach activities have been planned at several levels and dissemination to the general public involving participation of early-stage researchers. The CQUM has contact with local and national industries demonstrating ability to transfer of knowledge to the private sector. Most of the activity is developed with local industries and national and international patents have been released.

CQUM infrastructure is used daily by more than 150 researchers, including integrated researchers, graduate, MSc and PhD students, project grant researchers or technical staff. In the

period 2018-2023, young researchers became active members of CQUM under FCT CEEC (Call to Scientific Employment Stimulus) program and integrated in areas of research that were previously identified as strategic (for example molecular modelling to complement drug design know-how). CQUM reinforced human resources with a technician that contributes to improving the management and operational conditions of the current analytical equipment and broadens the services that CQUM can supply to external entities. CQUM also participates in networks (for example *PT-OPENSCREEN,* CryoEM) that could be considered a reference at a national or international level.

Currently, there are 30 ongoing projects led and participated by CQUM researchers, funded by entities such as FCT, ANI, and PRR, involving partners from other UMinho's R&D units, other national and international research units and external entities.

The research momentum and experience gathered in the 2018-2023 period have launched the foundations for the following funding period between 2025-2029. The team at CQUM is deeply engaged in transforming CQUM into a research unit of excellence and a reference at the national and international level.