



# BBPore2025

**I Conference on Biotechnological  
and Biomedical Applications  
of Porous Materials**

[www.icmol.es/bbpore2025/](http://www.icmol.es/bbpore2025/)

**8 and 9 May 2025,  
Valencia, Spain**



## BBPore2025

**I Conference on Biotechnological and  
Biomedical Applications of Porous Materials**



**THURSDAY 8TH MAY**

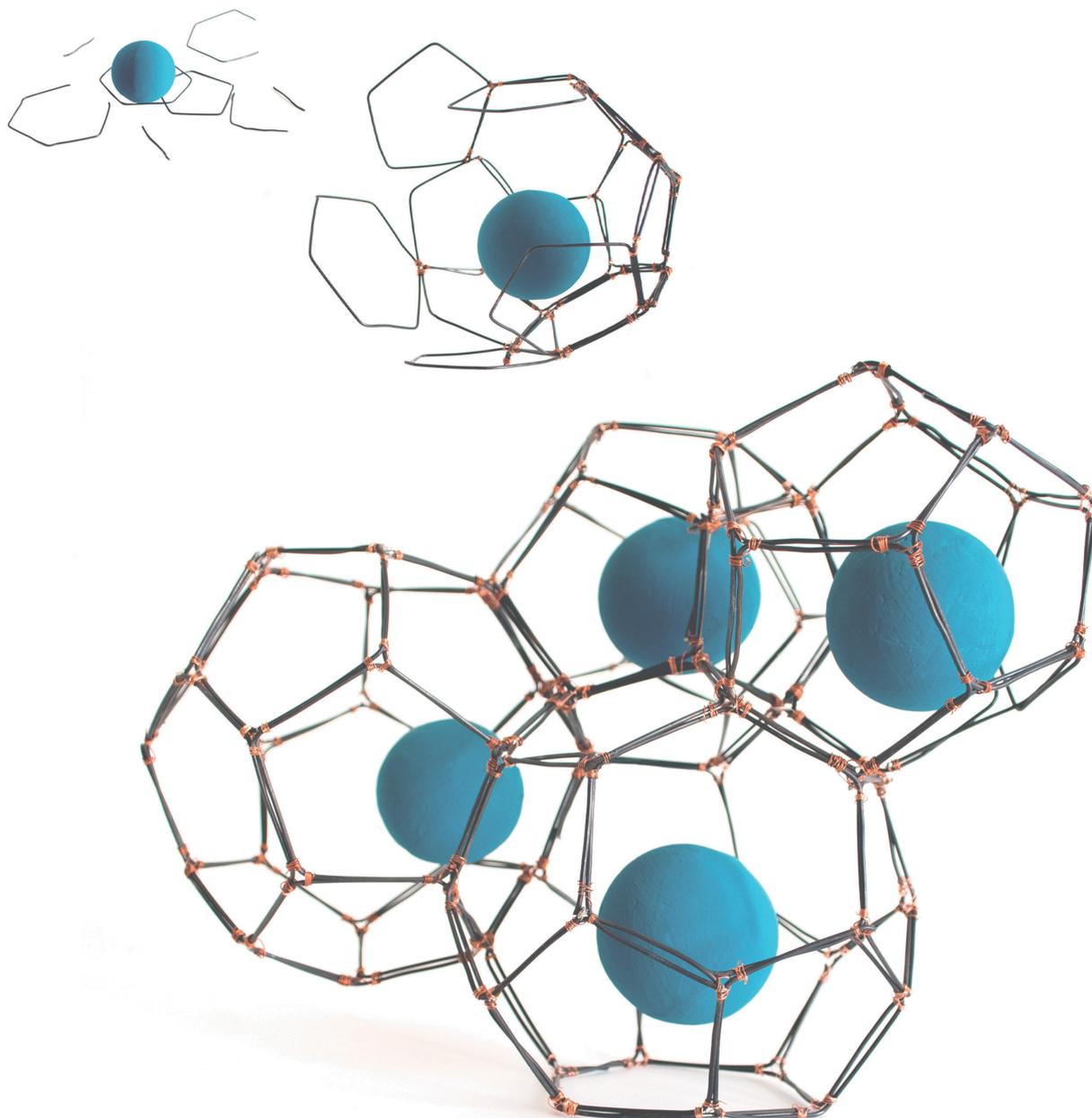
09:00 Welcome

**CHAIR 1**09:15 **Patricia Horcajada**09:55 **Beatriz Pelaz**10:25 **Oral Comm. 1-2**  
Mathilde Lepoitevin  
Tania Hidalgo11:05 **COFFEE**11:50 **Paolo Falcaro**12:30 **Oral Comm. 3 - 5**  
Jana Glatz  
Guillermo Moreno  
Mary Cano-Sarabia13:30 **Flash presentations 1-4**  
Jesús Cases  
Darragh McHugh  
Rocío López Lima  
M.<sup>a</sup> Dolores Garrido14:00 **LUNCH**15:15 **Clémence Sicard**15:45 **Carlos Martí-Gastaldo**16:15 **Oral Comm. 6 - 7**  
Manuel Ceballos  
Héctor Martínez-Pérez16:55 **BREAK**17:25 **Christian Serre**18:05 **Oral Comm. 8 - 9**  
Giulia Zampini  
Sumanta Chowdhury18:45 **Flash Presentations 5 - 8**  
Samuel Funes-Hernando  
Miquel Martínez  
Xuefan Chen  
Nikolaos Liodakis19:15 **COCKTAIL DINNER****FRIDAY 9TH MAY**09:00 **David Fairen-Jiménez**09:40 **Francesco Carraro**10:10 **Oral Comm. 10 - 11**  
Vicente Martí Centelles  
Ana María Borrego10:50 **COFFEE**11:30 **Sara Rojas**12:00 **Oral Comm. 12 - 13**  
Jesús Ferrando Soria  
Andrea Laybourn12:40 **Ross Forgan**13:30 **LUNCH**14:30 **Closing remarks**

# Index

---

Organizing committee	5
Invited Lectures	6
Program 8th May	8
Program 9th May	12
Abstracts	14



# Organizing committee

---

# BBPORE2025



**Mónica Giménez-Marqués**

Instituto de Ciencia Molecular (ICMol) of the Universitat de València



**Guillermo Mínguez Espallargas**

Instituto de Ciencia Molecular (ICMol) of the Universitat de València



**Francesco Carraro**

Instituto de Ciencia Molecular (ICMol) of the Universitat de València



[www. icmol.es/bbpore2025/](http://www.icmol.es/bbpore2025/)

**Venue: Centre Cultural  
la Nau - Valencia, Spain**

# Invited Lectures

#BBPORE2025



**Paolo Falcaro**

TU Graz, Austria



**David Fairen-Jimenez**

University of Cambridge, UK



**Patricia Horcajada**

IMDEA Energy, Spain



**Ross Forgan**

University of Glasgow, UK



**Christian Serre**

Institut of Porous Materials of  
Paris, France



**Sara Rojas**

University of Granada, Spain



**Francesco Carraro**

TU Graz, Austria



**Clemence Sicard**

Institut Lavoisier, France



**Beatriz Pelaz**

CiQUS USC, Spain



**Carlos Marti**

Institute of Molecular Science,  
Spain



**speakers**

# Event Schedule

Thursday 8th May

9:00	<b>Welcome</b>
9:15	<b>Patricia Horcajada</b> <i>IMDEA Energy</i> Smart Drug Nanocarriers: Harnessing the Synergy of Inorganic Nanoparticles and Metal-Organic Frameworks in Nanocomposites
9:55	<b>Beatriz Pelaz</b> <i>Center for Research in Biological Chemistry and Molecular Materials (CiQUS)</i> Nanosized-MOFs for live cell applications
	<b>Oral Communications 1-2</b>
10:25	<b>Mathilde Lepoitevin</b> <i>Institut of Porous Materials (IMAP)</i> Metal-Organic Frameworks: Pioneering Advanced Antibacterial Solutions for Wound Healing
	<b>Tania Hidalgo</b> <i>IMDEA Energy</i> Anti-COVID MOFs: unconventional nanoweapon
11:05	<b>Coffee break</b>
11:50	<b>Paolo Falcaro</b> <i>Graz University of Technology</i> ZIF Biocomposites: A Closer Look at the Synthesis–Property Relationship
12:30	<b>Oral Communications 3-5</b>

**Jana Glatz**

*Institute of Molecular Science*

Expanding the Pore, Expanding Possibilities: Biocompatible Frameworks for Overcoming Diffusion Limitations in Depolymerization

**Guillermo Moreno-Alcántar**

*Technical University of Munich*

Gold porphyrin metallacages: host-guest enabled G4 stabilization

**Mary Cano-Sarabia**

*ICN2 - Catalan Institute of Nanoscience and Nanotechnology*

Lipid/MOF biocomposites as delivery vehicles for hydrophobic drugs

**Flash presentations 1-4**

**F1: Jesús Cases**

Institute of Molecular Science

New synthetic strategies to access chemically diverse MOF biocomposites

**F2: Darragh McHugh**

*University of Galway*

OnG7: A Metal–Organic Framework for Potential Chemotherapeutic Delivery in Breast Cancer Treatment

**F3: Rocío López Lima**

*Polytechnic University of Valencia*

Supramolecular Strategies for Guest Encapsulation and Release at the Molecular Scale

**F4: María Dolores Garrido Blay**

*Institute of Materials Science (ICMUV)*

Atrane-Based Synthesis of Potential Theranostic Mesoporous Silica Materials for MRI and XFCT Imaging

**13:30**

<b>14:00</b>	<b>Lunch</b>
<b>15:15</b>	<p><b>Clémence Sicard</b> <i>Institut Lavoisier de Versailles</i></p> <p>Application of Metal-Organic Frameworks encapsulating biological entities as adjuvants in prophylactic vaccine formulations</p>
<b>15:45</b>	<p><b>Carlos Martí-Gastaldo</b> <i>Institute of Molecular Science</i></p>
	<b>Oral Communications 6-7</b>
<b>16:15</b>	<p><b>Manuel Ceballos Guzman</b> <i>Universidade de Santiago de Compostela</i></p> <p>Controlled Growth of PCN-224 on Plasmonic Nanoparticles: Engineering Photoactive Microporous Nanocarriers</p>
	<p><b>Héctor Martínez-Pérez-Cejuela</b> <i>University of Valencia</i></p> <p>Metal–Organic Frameworks in (Bio)Sensing: Integrating Luciferases and Nanozymes for Robust Analytical Platforms</p>
<b>16:55</b>	<b>Coffee break</b>
<b>17:25</b>	<p><b>Christian Serre</b> <i>Institut of Porous Materials (IMAP)</i></p> <p>Fe-MOFs to treat bacterial infections</p>
	<b>Oral Communications 8-9</b>
<b>18:05</b>	<p><b>Giulia Zampini</b> <i>Center for Research in Biological Chemistry and Molecular Materials (CiQUS)</i></p>

Surface Functionalization of Zirconium-Based MOFs with Phosphate-Containing Bioactive Molecules for Targeted Cellular Interactions

**Sumanta Chowdhury**

*Nantes University*

Surface Functionality in NanoCOFs Drives Enhanced Cellular Uptake in Lung Cancer Cells

**Flash presentations 5-8**

**F5: Samuel Funes-Hernando**

*Center for Research in Biological Chemistry and Molecular Materials (CiQUS)*

Protein adsorption and thermal protection within the mesopores of a nano-Hierarchical-MOF (H-UiO-66-NH<sub>2</sub>)

**F6: Miquel Martínez**

*University of Valencia*

Ultraflexible Liposomal Nanoplatfoms for Vitamin B12 Delivery in Advanced Skin Disease Therapies

**18:45**

**F7: Xuefan Chen**

*University of Valencia*

Molecular Insights into Cyclosporine Adsorption on Montmorillonite: A Computational Approach

**F8: Nikolaos Liodakis**

*Center for Research in Biological Chemistry and Molecular Materials (CiQUS)*

Synthesis of highly crystalline imine-based COF nanospheres with tunable sizes

**19:15**

**Cocktail dinner**

## Friday 9th May

9:00	<p><b>David Fairen-Jiménez</b> <i>University of Cambridge</i> Translation of Nanomaterials for Hard-to-Treat Cancer</p>
9:40	<p><b>Francesco Carraro</b> <i>Graz University of Technology</i> Hydrogen-bonded Organic Frameworks for biotechnology applications</p>
10:10	<p><b>Oral Communications 10-11</b></p>
	<p><b>Vicente Martí Centelles</b> <i>Polytechnic University of Valencia</i> Tailoring Molecular Cages for Guest Binding, Sensing, and Biomedical Applications</p>
	<p><b>Ana María Borrego</b> <i>University of Valencia</i> Sepiolite as a porous nanocarrier to enhance mirtazapine drug delivery</p>
10:50	<p><b>Coffee break</b></p>
11:30	<p><b>Sara Rojas</b> <i>University of Granada</i> Metal-Organic Frameworks as multifunctional platform in agriculture</p>
12:00	<p><b>Oral Communications 12-13</b></p>
	<p><b>Jesus Ferrando Soria</b> <i>Institute of Molecular Science</i> Bio-Metal-Organic Frameworks for the Removal of Emergent Contaminants</p>

**Andrea Laybourn**

*University of Leeds*

Scalable and Sustainable Synthesis of Metal-Organic Frameworks and Magnetic Framework Composites for Biomedical Applications

**12:40**

**Ross Forgan**

*University of Glasgow*

**13:30**

**Lunch**

**14:30**

**Closing remarks**

# Abstracts



# Abstracts

---

Plenary and invited	15
Oral communications	23
Flash presentations	36

# Smart Drug Nanocarriers: Harnessing the Synergy of Inorganic Nanoparticles and Metal-Organic Frameworks in Nanocomposites

Darina Francesca PICCHI, Sorraya LELOUCHE, Catalina BIGLIONE, **Patricia HORCAJADA**

<sup>a</sup>*Advanced Porous Materials Unit, IMDEA Energy Institute, Móstoles, Madrid*

e-mail: [patricia.horcajada@imdea.org](mailto:patricia.horcajada@imdea.org)

**Keywords:** *MOF, inorganic nanoparticles, nanocomposites, drug delivery systems, antitumoral drugs*

Metal-organic frameworks (MOFs) are currently recognized as promising drug delivery systems (DDS), showcasing biocompatibility, substantial drug loadings, and controlled release capabilities. [1] In a recent development, an exciting avenue has emerged by integrating MOFs with plasmonic or magnetic inorganic nanoparticles (iNPs) to achieve controlled drug release triggered by light or magnetism in both spatial and temporal dimensions. Furthermore, the inclusion of iNPs imparts these nanocomposites with a range of compelling properties, including photodynamic therapy (PDT), magnetofection, magnetic hyperthermia/photothermal therapy (PTT), and applications such as magnetic resonance imaging (MRI), or biosensing, among others. Additionally, the combination with biocompatible MOFs serves to stabilize the iNPs, further enhancing the overall performance of these composite materials. [2-4]

In this presentation, we will describe the preparation of several iNP@MOF nanocomposites designed for triggered drug release and/or combined therapies

## References

- [1] S. Rojas et al., *Coord. Chem. Rev.*, **2019**, 388, 202-226; M. Giménez-Marqués, et al., *Coord. Chem. Rev.*, **2016**, 307, 342–360.
- [2] D. F. Picchi et al., *ACS Nanosci. Au*, **2023**, 10.1021/acsnanoscienceau.3c00041; C. Carrillo-Carrión et al., *Angew. Chem. Int. Ed.* **2019**, 58, 7078–7082; S. N. K. Lelouche, et al., *Expert Opinion on Drug Delivery*, **2022**, 19:11, 1417-1434; A. G. Skirtach, et al., *Angew. Chem. Int. Ed.* **2006**, 45, 4612; S. Carregal-Romero et al., *Nanoscale*, **2015**, 7, 570.
- [3] S. Persano, *Cancers (Basel)*, **2021**, 13 (11), 1–31; C. Biglione, et al., *Nanoscale*, **2020**, 12.42: 21635-21646.

# Nanosized-MOFs for live cell applications

**Beatriz PELAZ**

<sup>1</sup> *CiQUS, Universidade de Santiago de Compostela, 15782 Santiago de Compostela, Spain.*  
E-mail: beatriz.pelaz@usc.es

Metal-organic frameworks (MOFs) have emerged as highly versatile materials due to their tunable porosity, structural diversity, and functionalization capabilities. When synthesized at the nanometric scale (nanoMOFs, NMOFs), they can be used as nanocarriers to explore their interaction with living entities. This interaction is highly determined by their size, shape and surface modification.

Moreover, their integration into advanced nano-composites allows the combination of their unique properties with the properties of inorganic nanoparticles, i.e., gold nanoparticles, metallic, etc., expanding their potential applications as remotely-controlled nanosystems. We will discuss nanoMOF-based composites and their applications in biological systems as smart nanocarriers.

We will discuss the synthesis and surface modification strategies of nanoMOFs to enhance their biocompatibility and stability. These strategies will cover the use of different surface modification strategies such as the use of polymers or biomimetic systems.

Our findings demonstrate that nanoMOFs and nano-composited MOF-based materials offer significant advantages, providing multifunctionality and enhanced performance for biomedical applications. The use of nano-sized MOFs represents a promising avenue for the development of next-generation materials with tailored functionalities for healthcare and biotechnology.

# **ZIF Biocomposites: A Closer Look at the Synthesis–Property Relationship**

Paolo **FALCARO**<sup>1</sup>, Michael HAFNER<sup>1</sup>, Francesco CARRARO<sup>1</sup>, Christian DOONAN<sup>1,2</sup>

<sup>1</sup>*Institute of Physical and Theoretical Chemistry, Graz University of Technology, Graz 8010, Austria*

<sup>2</sup>*Department of Chemistry, School of Physics Chemistry and Earth Sciences, The University of Adelaide, Adelaide, SA 5005, Australia*

Zeolitic Imidazolate Frameworks (ZIFs) have attracted significant attention in biomimetic mineralization, owing to their capacity to spontaneously form a protective coating around sensitive biomacromolecules and assemblies thereof. Different studies have shown that distinct ZIF phases can be obtained under varying synthetic conditions, and each individual phase exhibits distinct functional properties. Motivated by these observations, we systematically explored a substantial portion of the viable reaction space to establish an extended map of the domains of the most prominent ZIF phases. By varying precursor ratios, overall concentrations, and post-synthetic treatments, we constructed ternary phase diagrams that reveal how crystallinity, porosity, encapsulation efficiency, and loading capacity depend on the resulting phase. This expanded mapping provides new opportunities to design ZIF biocomposites with tunable properties for a wide range of biotechnological and therapeutic applications.

# Application of Metal-Organic Frameworks encapsulating biological entities as adjuvants in prophylactic vaccine formulations

Clémence SICARD

*Institut Lavoisier de Versailles, UVSQ, CNRS UMR 8180, Univ. Paris-Saclay, Versailles.*

*Institut Universitaire de France*

*E-mail: clemence.sicard@uvsq.fr*

Bio-entities benefit from unparalleled activities of high interest in many applications such as environmental and medical field. However, these are fragile entities, easily degraded under non-native conditions. Encapsulation, i.e. inclusion within a host matrix, is particularly interesting for bio-entities stabilization and protection, and Metal-Organic Frameworks (MOFs) have arisen as a host matrix of choice, resulting in the design of novel functional materials.[1] However, the number of MOF/bio-entities couples is limited either due to size matching constraints or to a narrow window of compatible synthetic conditions.

In this presentation, we will present our efforts to expand biocompatible synthetic routes to explore new compositions and structures of bio-entities-MOFs hybrids. We will briefly describe the synthesis and characterization of MOFs-based living materials, using the mesoporous iron polycarboxylate MIL-100(Fe).[2] We will also present our latest finding on the design of bio-entities@Al-MOF.[3] We will show that the bio-entities@Al-MOF act as a potent vaccine formulation as it demonstrated *in-vivo* a stronger adjuvant effect than the benchmark Al-adjuvant, was fully resorbable, disappearing from the injection site, was not exhibiting any toxicity, and was stable for two years.

## References:

[1] (a) E. Gkaniatsou *et al.*, *Mater. Horiz.* **2017**, 55; (b) R. J. Drout *et al.*, *Chem. Rev.* **2019**, 150, (c) X. Wang *et al.*, *ACS Cent. Sci.*, **2020**, 9; (d) S. Huang *et al.*, *Angew. Chem. Int. Ed* **2020**, 8786; (e) W. Liang *et al.*, *Chem. Rev.* **2021**, 1077.

[2] A. Permyakova *et al.*, *ACS Materials Letters*, **2023**, 79.

[3] (a) I. Christodoulou, *et al.*, *Inorganic Chemistry* **2025**, 64, 5, 2545–2553 (b) patent application WO/2022/207922 and I. Christodoulou, E. Gkaniatsou *et al.*, *ChemRxiv* **2023**.

# Fe-MOFs to treat bacterial infections

Christian SERRE

*Institut des Matériaux Poreux de Paris, Ecole Normale Supérieure, ESPCI Paris, CNRS,  
PSL University, 75005 Paris, France.*

E-mail: christian.serre@ens.psl.eu

Nanoparticles of biocompatible metal organic frameworks (nanoMOFs), due to their large drug loading capacities and controlled release properties, have shown promises in nanomedicine, mainly to treat cancer. Iron based nanosized MOFs, a sub-class of nanoMOFs, are particularly appealing due to their low toxicity, biodegradable character and (in some cases) their iron Lewis acid sites.<sup>[1]</sup>

The delivery of biological gases such as Nitric oxide (NO), a powerful therapeutic agent, is of interest in biomedicine due to its anti-thrombogenic or antibacterial properties, among others. Its utilization requires however the use of biocompatible carriers able to adsorb significant amounts of NO while delivering it on a controlled manner depending on each application.<sup>[2]</sup> MOFs have been previously proposed as gaso-transmitters due to the coordination of NO on their open metal sites while the release was ensured upon exposure to a wet gas. However, once in contact with body fluids, the release of NO occurs within minutes compromising in most cases their practical use while the current Fe-MOFs tend to leach out iron in solution, leading to potential toxicity issues.<sup>[2]</sup> We have recently reported highly stable biocompatible MOFs with an exceptional stability and exploited them for the controlled delivery of NO in body fluids. The biocompatible Ti-MOF MIP-177 can absorb and release NO within 2 hours in phosphate buffer, due to an unprecedented NO adsorption/release mechanism.<sup>[3]</sup> The ultra-microporous iron bisphosphonate MOF, denoted MIP-210, can release NO up to a record ca. 3 days in biological media without any metal leaching.<sup>[4]</sup> Such properties enable to use these MOFs as ‘porous liquids’ in order to ensure a prolonged cell migration or even angiogenesis, paving the way for the design of new wound healing therapies; or beyond towards applications where a prolonged release of NO in body fluids is required with minimal side toxicity effects.

A second strategy deals with the loading of NIR dyes into large pores Fe-MOFs for PTT/PDT therapy. While preventing from a bleaching of the dye under irradiation, we demonstrate how new MOF-dyes composites, through a multimodal based on PTT/PDT and chemo-dynamic strategy, are of interest to treat anti-biotic resistant infections.<sup>[4, 5]</sup> Finally, we will show first insights about nanosized Fe-MOF based composites with ferroptosis and drug therapy properties, that have been prepared under green ambient pressure conditions, to treat inflammatory diseases.<sup>[6-7]</sup>

## References

- [1] Z. Yu, M. Lepoitevin, C. Serre, *Adv. Healthcare Mat.*, **2024**; doi.org/10.1002/adhm.202402630
- [2] R. Pinto, M. Pinto, C. Serre, *Adv. Healthcare Mater.*, **2025**, in press, adhm.202404553R1
- [3] R.V. Pinto, S. Wang, S.R. Tavares, J. Pires, F. Antunes, A. Vimont, G. Clet, M. Daturi, G. Maurin, C. Serre, M.L. Pinto, *Angew. Chem. Int. Ed.*, **2020**, 59, 5135–5143.
- [3] R. V. Pinto, C.-C. Cao, P. Lyu, I. Dovgaliuk, C.-Y. Su, G. Maurin, F. Antunes J. Pires, V. André, C. Henriques, A. Tissot, M. L. Pinto and C. Serre; *Small*, **2024**, 2405649; <https://doi.org/10.1002/sml.202405649>
- [4] Z. Lu, T. Lucas, H. Zhao, C. Chen, I. Dubail, Y. Chen, G. Patriarche, J. Gateau, F. Gazeau A. Jamet, M. Lepoitevin, C. Serre, *Adv. Healthcare Mat.*, **2024**, doi.org/10.1002/adhm.202402418

- [5] X. Qi, E. Gafskaiia, Z. Yu, N. Shen, E. Fedina, A. Masyutin, M. Erokhina, M. Lepoitevin, V. Lazarev, N. Zigangirova, C. Serre, M. Durymanov, *ACS Infectious Diseases* **2023**, doi.org/10.1021/acsinfecdis.3c00131
- [6] H. Zhao, S. Sene, A. M. Mielcarek, S. Miraux, N. Menguy, D. Ihiwakrim, O. Ersen, C. Péchoux, N. Guillou, J. Scola, J.-M. Grenèche, F. Nouar, S. Mura, F. Carn, F. Gazeau, E. Dumas, C. Serre, and N. Steunou, *J. Mater. Chem. B*, **2023**, doi.org/10.1039/D2TB02094G
- [7] H. Zhao, S. Becharef, E. Dumas, F. Carn, G. Patriarche, S. Mura, F. Gazeau, C. Serre and N. Steunou, *Nanoscale*, **2024**, *16*, 12037-12049; doi.org/10.1039/D3NR06685A

# Hydrogen-bonded Organic Frameworks for biotechnology applications

**Francesco CARRARO**

*Institute of Physical and Theoretical Chemistry, Graz University of Technology, Graz 8010,  
Austria*

E-mail: Francesco.carraro@tugraz.at

Recently, Hydrogen-bonded Organic Frameworks (HOFs) emerged as a matrix for preparing enzyme biocomposites in biocompatible synthesis conditions (e.g., room temperature and water).[1] The examples reported so far have shown performances superior to other supported-enzyme systems in terms of protein protection and loading capacity, and wide pH range stability. However, the possibility of imparting additional functional properties to these promising biocatalysts by preparing multi-component enzyme@HOF biocomposites is still at its infancy. The talk will focus on our recent studies in this research area, in particular on i) the integration of magnetically responsive nanoparticles in HOF biocomposites as an attractive strategy to impart dynamic localization properties and to develop microfluidic biosensors, and ii) on innovative solid-state syntheses of HOF biocomposites.[2,3]

[1] W. Liang, F. Carraro, M. B. Solomon, S. G. Bell, H. Amenitsch, C. J. Sumby, N. G. White, P. Falcaro, C. J. Doonan, *J. Am. Chem. Soc.* 2019, 141, 14298.

[2] F. Carraro, M. Aghito, S. Dal Zilio, H. Wolinski, C. J. Doonan, B. Nidetzky, P. Falcaro, *Small* 2024, 2407487.

[3] M. Hafner, N. Pantalon Juraj, K. Flint, H. Wiltsche, H. Amenitsch, C. J. Doonan, K. Uzarevic, F. Carraro, 2025, 10.26434/chemrxiv-2025-x484t

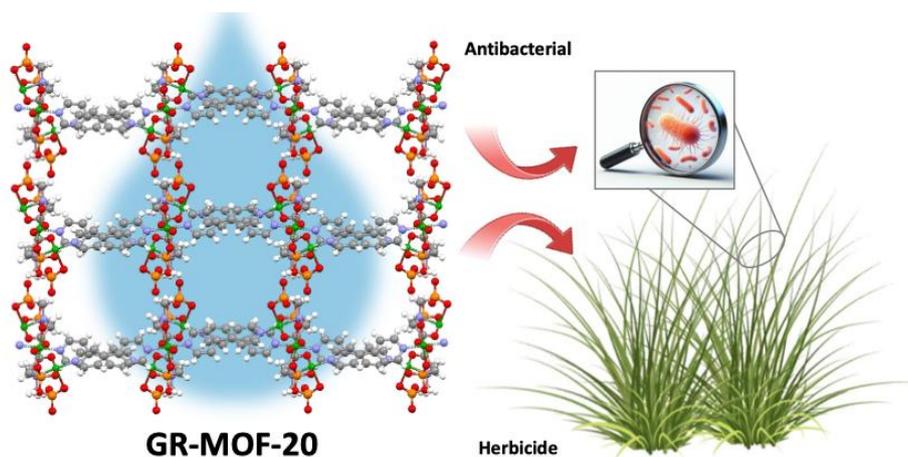
# Metal-Organic Frameworks as multifunctional platform in agriculture

Sara ROJAS, Samuel MORALES-CÁMARA, MCarmen CONTRERAS, Pablo SALCEDO-ABRAIRA, Antonio RODRÍGUEZ-DIÉGUEZ

<sup>1</sup> Department of Inorganic Chemistry, University of Granada, Granada/Spain  
E-mail: srojas@ugr.es

The convergence of population growth and climate change threatens food security on a worldwide scale. Current trends in population growth suggest that global food production is unlikely to satisfy future demand as predicted. In order to accomplish these significant objectives, the use of agrochemicals (fertilizers, pesticides, plant hormones, etc.) becomes inevitable to ensure quality and high yields. However, their intensive application has resulted in the deterioration of ecosystems, making necessary to develop more efficient and less toxic methods against pests and infections, while improving crops productivity. Importantly, large quantities of agrochemicals do not reach their intended objectives due to application practices (between 10-75% do not reach their target) and their widespread use, contributing to the deterioration of ecosystem quality, adversely affecting the health of living beings, water and soil.

Among the novel technologies considered, Metal-Organic Frameworks (MOFs) appeared as innovative and promising materials for environmental applications.[1] In this work, we take a further step and use organic agrochemicals as linkers in the preparation of MOFs, what we have called AgroMOFs (Figure 1). Through this original strategy, we aim to achieve a controlled agrochemical delivery and enhance crop production and quality, while reducing contamination.[2] All these studies evidenced the potential of MOFs in agriculture without damaging our environment.



**Figure 1.** GR-MOF-20 based on  $\text{Cu}^{2+}$  and glyphosine, and its dual effect as antibacterial and herbicidal agent.

## Acknowledgments

MOFCycle (CNS2022-135779), POR4Water (PLSQ\_00188) and ProyExcel\_00105 projects, FQM-394, and the Ramón y Cajal program (RYC2021-032522-I).

## References

[1] Rojas, S; Horcajada, P; Metal–Organic Frameworks for the Removal of Emerging Organic Contaminants in Water. *Chem. Rev.* **2020**, 120, 16, 8378-8415.

[2] Sierra-Serrano, B; García-García, A; et al. Copper Glufosinate-Based Metal–Organic Framework as a Novel Multifunctional Agrochemical. *ACS Appl. Mater. Interfaces* **2022**, 14, 34955-34962.

## Metal-Organic Frameworks: Pioneering Advanced Antibacterial Solutions for Wound Healing

Mathilde LEPOITEVIN,<sup>1</sup> Xiling SONG,<sup>1</sup> Zhihao YU,<sup>1</sup> Xiali FU,<sup>2</sup> Anne JAMET,<sup>2</sup>  
Christian SERRE,<sup>1</sup>

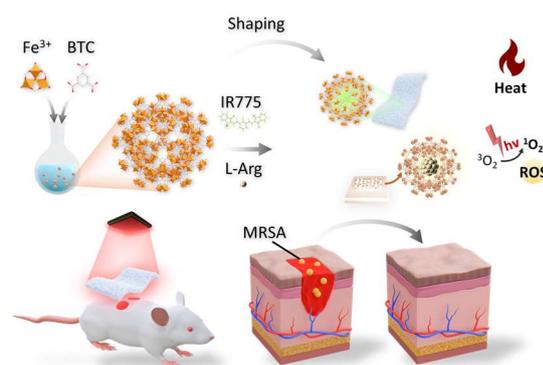
<sup>1</sup>IMAP, ENS, ESPCI, CNRS, PSL, 24 rue Lhomond, Paris, France.

<sup>2</sup>Université Paris Cité, INSERM, CNRS, Institut Necker Enfants Malades, Paris, France

e-mail: [mathilde.lepoitevin@ens.fr](mailto:mathilde.lepoitevin@ens.fr)

The rise of antibiotic-resistant bacteria necessitates innovative approaches for infection control and wound healing. This study explores metal-organic frameworks (MOFs)[1] as multifunctional platforms for antibacterial therapy, integrating photothermal/photodynamic therapy (PTT/PDT) and controlled nitric oxide (NO) release. [2]

We present MIL-100(Fe)@IR775 nanoparticles synthesized via a green method,[3] exhibiting enhanced photostability and potent antibacterial activity against MRSA under LED irradiation.[4] The MOF structure prevents photobleaching and aggregation-induced quenching, ensuring repeated photothermal treatment. In vitro and in vivo studies demonstrate up to 98.5% bacterial eradication and accelerated wound healing. Additionally, MIL-100(Fe)@L-arginine microneedles enable controlled NO release. L-arginine, encapsulated within MIL-100(Fe), reacts with hydrogen peroxide produced by lactate oxidase, generating NO and hydroxyl radicals for synergistic antibacterial action. This dual approach significantly enhances bacterial clearance and wound repair.



Scheme of the MOF-enhanced dressings for drug-resistant bacteria in wound care

These findings position MOF-based platforms as promising alternatives for treating drug-resistant infections and improving wound care. The combination of phototherapy and NO-based treatment offers a versatile and effective strategy for next-generation antibacterial therapies.

[1] a. Ma, X., Lepoitevin, M., & Serre, C. Metal–organic frameworks towards bio-medical applications. *Materials Chemistry Frontiers*, **2021**, 5(15), 5573–5594. b. Yu, Z., Lepoitevin, M., & Serre, C. Iron-MOFs for Biomedical Applications. *Advanced Healthcare Materials*, **2025**, 2402630.

[2] Pinto, R. v., Wang, S., Tavares, S. R., Pires, J., Antunes, F., Vimont, A., Clet, G., Daturi, M., Maurin, G., Serre, C., & Pinto, M. L. Tuning Cellular Biological Functions Through the Controlled Release of NO from a Porous Ti-MOF. *Angewandte Chemie International Edition*, **2020**, 59(13), 5135–5143.

[3] Ma, X., Yu, Z., Nouar, F., Dovgaliuk, I., Patriarche, G., Sadovnik, N., Daturi, M., Grenèche, J. M., Lepoitevin, M., & Serre, C. How Defects Impact the In Vitro Behavior of Iron Carboxylate MOF Nanoparticles. *Chemistry of Materials*, **2024**, 36(1).

[4] Yu, Z., Fu, X., Lucas, T., Zhao, H., Chen, C., Dubail, I., Chen, Y., Patriarche, G., Gateau, J., Gazeau, F., Jamet, A., Lepoitevin, M., Serre, C. MOF-Enhanced Phototherapeutic Wound Dressings Against Drug-Resistant Bacteria. *Advanced Healthcare Materials*, **2025**, 14(1), 2402418.

## Anti-COVID MOFs: unconventional nanoweapon

Beatrice FODOR<sup>a</sup>, Inés ÁLVAREZ-MIGUEL<sup>a</sup>, Catalina BIGLIONE<sup>a</sup>, Guillermo GUTIÉRREZ<sup>a</sup>, África GONZÁLEZ-FERNÁNDEZ<sup>b,c</sup>, Fabrice SALLES<sup>d</sup>,  
**Tania HIDALGO<sup>a\*</sup>**, Patricia HORCAJADA<sup>a\*</sup>

<sup>a</sup>IMDEA Energy Institute, Advanced Porous Materials Unit (APMU), 28935 Móstoles, Spain.

<sup>b</sup>CINBIO, Immunology Group, University of Vigo, 36310 Vigo, Spain

<sup>c</sup>Galicia Sur Health Research Institute (IIS Galicia Sur), SERGAS-UVIGO, Spain.

<sup>d</sup>ICGM, University of Montpellier, CNRS ENSCM, Montpellier, France

E-mail: tania.hidalgo@imdea.org

SARS-CoV-2 (COVID-19) pandemic outbreak had led towards to epical socioeconomic repercussions worldwide over the past years (>770 million of infections, ~7 million of deaths &/or >€8 trillion of economic burden), making imperative the design of new therapies to combat this fastest-spreading virus in the world history.<sup>[1]</sup> In this context, nanomedicine has risen as a promising tool to treat challenging diseases (eg. cancer), including viral or bacterial infections.<sup>[2]</sup> In particular, Metal-organic frameworks (MOFs), constituted by metal centres or clusters that are bonded to polydentate ligands, have emerged as original and effective alternative drug delivery systems.<sup>[3]</sup> Despite their features, previous therapeutic outcomes with other pathologies or their recent approach in sensing for COVID-19 detection or biomedicine for drug release,<sup>[4]</sup> MOFs have not been deeply investigated for the antiviral purposes. Hence, we propose a pioneer intrinsic nanoMOF role in a combined anti-COVID multi-therapy (3-in-1 effect) by their pulmonary administration.

In this sense, we have prepared 7 diverse compositional & topological nanoscaled MOFs with potential intrinsic antiviral activity (*effect 1*). By the screening of their biocompatibility and antiviral activity against SARS-CoV-2 infected human cell lines (A549-ACE2), the best performing nanomaterial was selected (IC50: <2 µM; cell viability >99%) for the encapsulation of an antiviral drug (Favipiravir; 21±3 wt%), providing complementary antiviral and chemotherapeutic activity (*effect 2*).<sup>[5]</sup> In addition, to fulfil our strategy, a heparin grafting was conducted, achieving greater antiviral action at lower concentrations (IC50:<1 µM) due to proven immune- and/or chemotherapeutic activity against the SARS-CoV-2 (*effect 3*).<sup>[6]</sup> Lastly, mannitol-based microspheres were prepared using the 3-in-1 system as an efficient pulmonary formulation,<sup>[7]</sup> reaching the deepest zones of the lung in absence of toxicity in a murine model. Besides, a substantial cytokines secretion was evidenced even at shorter times (eg. pro-inflammatory, IL-6, IL-10), being able to modulate the immune response upon inhalation.

In short, the successful development of this MOF-based formulation along with its demonstrated antiviral activity and biosafety in a real infected human cellular scenario, plus the capability to modulate the immune response at the *in vivo* level, marks a significant step forward in the antiviral therapeutics approach. These findings open new avenues for further MOF exploration in antiviral therapies/prophylaxes, offering a powerful new tool in the fight against global pandemics.

### Acknowledgment

“Community of Madrid” and European Regional Development Fund—FEDER 2014-2020-OE REACT-UE 1—financial support to the VIRMOF-CM project associated with R&D projects in response to COVID-19. T.H. thanks to grant PID2023-146253NA-I00 funded by MICIU/AEI/10.13039/501100011033 and by the “European Union NextGenerationEU/PRTR”.

### References

- [1] WHO Coronavirus Disease (COVID-19) Dashboard. 2024
- [2] Zeinali, S.; Moafian, Z.; Arshad, R.; Karimi, F; Zeinalilathori, S.; Rahdar, A.; Fathikarkan, S.; S. Pandey. *Springer US* **2024**.
- [3] Rojas, S.; Arenas-Vivo, A.; Horcajada, P. *Coord. Chem. Rev.* **2019**, 388, 202.
- [4] Plastiras, O. E.; Bouquet, P.; *et al. Mater. Today Bio* **2024**, 28, 101165.
- [5] Ghasemnejad-Berenji M.; Pashapour, S. *Drug Res.* **2021**, 71, 166.
- [6] Gelbach, A.; Zhang, F.; *et al. Front. Mol. Biosci.* **2022**, 9, 912887.
- [7] Fernández-Paz, C.; Rojas, S.; *et al. ACS Appl. Mater. Interfaces* **2020**, 12, 25676.

## Expanding the Pore, Expanding Possibilities: Biocompatible Frameworks for Overcoming Diffusion Limitations in Depolymerization

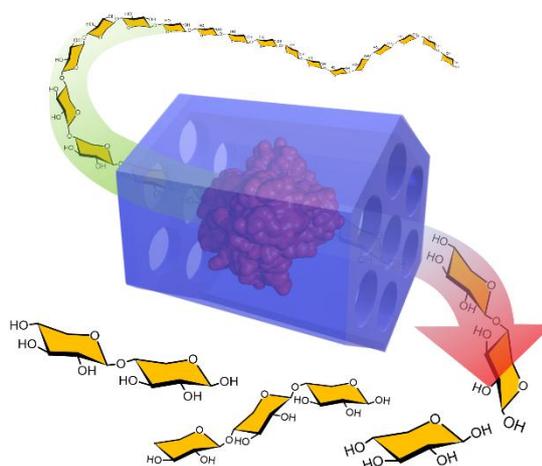
Jana Glatz<sup>1</sup>, Jesús Cases Díaz<sup>1</sup>, Jorge Salinas-Uber<sup>1</sup>, David Talens-Perales<sup>2</sup>,  
Julio Polaina<sup>2</sup> and Mónica Giménez-Marqués<sup>1</sup>

<sup>1</sup> Universidad de Valencia - Instituto de Ciencia Molecular, Avda. Catedrático José Beltrán  
Martínez 2, 46980 Paterna, Spain

<sup>2</sup> Instituto de Agroquímica y Tecnología de Alimentos (CSIC), Avda. Catedrático Agustín  
Escardino 7, 46980 Paterna, Spain

E-mail: jana.glatz@uv.es

The controlled synthesis of metal–organic frameworks (MOFs) under mild conditions has enabled the formation of hybrid biocomposites with potential application in biocatalysis.<sup>[1]</sup> Although the encapsulation of enzymes typically preserves their structural integrity and bioactivity, enhancing mass transport through the porous architecture remains a critical challenge<sup>[2]</sup>. However, integrating MOFs with large accessible porosity as protective scaffolds offers significant potential to improve enzymatic performance in depolymerization reactions, thereby advancing biocatalytic applications. Therefore, our research has been focused on developing a biocompatible and scalable synthetic method of a phase-pure aluminum trimesate porous framework, MIL-110(Al), which features large microporous channels. The method is compatible with the *in situ* enzyme encapsulation *via* a Lewis acid-mediated mineralization<sup>[3]</sup>, achieving high encapsulation efficiencies and controlled protein loading. Furthermore, we demonstrate a favored channel-directed depolymerization in a model biocomposite, xylanase@MIL-110(Al), which successfully hydrolyses the xylan polymer over consecutive cycles.



Schematic depolymerization reaction of xylan polymer using large-channeled MOF biocomposite

### References:

- [1] Liang, K.; Ricco, R.; Doherty, C. M.; Styles, M. J.; Bell, S.; Kirby, N.; Mudie, S.; Haylock, D.; Hill, A. J.; Doonan, C. J.; Falcaro, P. Biomimetic Mineralization of Metal–Organic Frameworks as Protective Coatings for Biomacromolecules. *Nat Commun* **2015**, *6* (1), 7240.
- [2] Hsu, P.-H.; Chang, C.-C.; Wang, T.-H.; Lam, P. K.; Wei, M.-Y.; Chen, C.-T.; Chen, C.-Y.; Chou, L.-Y.; Shieh, F.-K. Rapid Fabrication of Biocomposites by Encapsulating Enzymes into Zn-MOF-74 via a Mild Water-Based Approach. *ACS Appl. Mater. Interfaces* **2021**, *13* (44), 52014–52022.
- [3] Cases Díaz, J.; Lozano-Torres, B.; Giménez-Marqués, M. Boosting Protein Encapsulation through Lewis-Acid-Mediated Metal–Organic Framework Mineralization: Toward Effective Intracellular Delivery. *Chem. Mater.* **2022**, *34* (17), 7817–7827.

## Gold porphyrin metallacages: host-guest enabled G4 stabilization

Guillermo MORENO-ALCÁNTAR<sup>1</sup>, Tamara RODRÍGUEZ-PRIETO,<sup>1</sup> Darren WRAGG,<sup>1</sup>  
Roland A. FISCHER,<sup>1</sup> Angela CASINI<sup>1</sup>

<sup>1</sup> Technical University of Munich, Department of Chemistry, Lichtenbergstr. 4, 85748 Garching  
b. München, Germany  
E-mail: g.moreno-alcantar@tum.de

Self-assembled metallacages are emerging promising supramolecular systems that have shown potential in different fields of chemistry, including being developed as versatile platforms for biomedical applications, such as drug delivery, tumour therapy, bioimaging, and biosensing.[1] Such 3-dimensional metal-containing assemblies possess cavities that can accommodate various guest molecules (e.g. anti-cancer drugs, radiopharmaceuticals or imaging agents). By the correct design of the ligands and exploiting the predictable and well-defined coordination geometries of transition metal ions, the cage's size, and chemical-physical properties can be tuned to promote specific host-guest interactions [2].

Furthermore, the choice of bioactive building blocks can embed the 3-dimensional structures with further therapeutic and diagnostic properties. Recently we have developed the first gold(III) porphyrin-based self-assembled metallacage (**AuCg**), exploring its potential as a bioactive agent [3] and highlighting its selectivity as a guanine-quadruplex (G4) stabilizer (Figure 1). Importantly, our studies unveil the until-now overlooked significance of the host-guest chemistry in the stabilization of G4s. More recently, we have expanded our studies to other kinds of systems, porphyrin prisms, that also present enhanced G4 stabilization properties when gold is coordinated in the porphyrin. These findings support the positive effects of the inclusion of gold porphyrins in metallacages designed as G4 stabilizers.

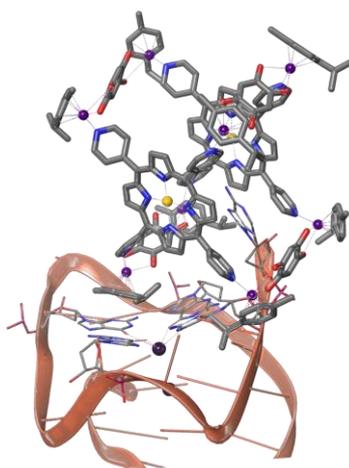


Figure 1. Interaction of **AuCg** with the C-KIT1 promoter G4.

### References

- [1] Moreno-Alcántar, G.; Casini, A. Bioinorganic Supramolecular Coordination Complexes and Their Biomedical Applications. *FEBS Lett.* **2023**, 597 (1), 191–202.
- [2] Tateishi, T.; Yoshimura, M.; Tokuda, S.; Matsuda, F.; Fujita, D.; Furukawa, S. Coordination/Metal–Organic Cages inside Out. *Coord. Chem. Rev.* **2022**, 467, 214612.
- [3] Rodríguez-Prieto, T.; Wragg, D.; Heiduk, N.; Park, M.; Strittmatter, N.; Fischer, R. A.; Casini, A.; Moreno-Alcántar, G. A Golden Touch in the Design of Multifunctional Porphyrin Metallacages: Host–Guest Chemistry for Drug-Target Interactions. *CCS Chem.* **2024**, 6 (7), 1662–1671.

## Lipid/MOF biocomposites as delivery vehicles for hydrophobic drugs

Mary Cano-Sarabia<sup>1</sup>, Paolo Falcaro<sup>2</sup>, Inhar Imaz<sup>1,3</sup>, Daniel MasPOCH<sup>1,3,4</sup>

<sup>1</sup> Catalan Institute of Nanoscience and Nanotechnology (ICN2), CSIC and The Barcelona Institute of Science and Technology, Campus UAB, Bellaterra 08193, Barcelona, Spain

<sup>2</sup> Institute of Physical and Theoretical Chemistry, Graz University of Technology, Graz 8010, Austria

<sup>3</sup> Departament de Química, Facultat de Ciències, Universitat Autònoma de Barcelona, Bellaterra 08193, Spain

<sup>4</sup> ICREA, Pg. Lluís Companys 23, Barcelona 08010, Spain

E-mail: mary.cano@icn2.cat

Over the past two decades, metal-organic framework (MOF) nanoparticles have garnered significant attention as efficient carriers for drug, nucleic acid, protein, and gene delivery applications. Their well-defined crystalline porous structures, high loading capacity, controlled release properties, low toxicity, and ease of chemical functionalization make them highly promising for biomedical use. However, their stability in biological environments, as well as the bioavailability, efficacy, and pharmacokinetic/pharmacodynamic control of their cargo, remain key challenges. In this study, we introduce a novel drug delivery system (DDS) that integrates lipid self-assemblies with MOFs to create biocomposites optimized for encapsulation, protection, and controlled release of functional molecules [1]. We report the one-pot synthesis of zeolitic imidazolate framework-8 (ZIF-8) MOF particles in the presence of lipid assemblies, forming various hybrid lipid/ZIF-8 biocomposites. This strategy facilitates the high-yield encapsulation of astaxanthin—an unstable, water-insoluble antioxidant known for its antiproliferative, neuroprotective, and anti-inflammatory properties, particularly in the treatment of Alzheimer’s disease. The resulting DDS demonstrates excellent *in vitro* cytocompatibility, antioxidant activity, and enhanced colloidal stability in biological media. The gastrointestinal digestion of astaxanthin was evaluated using the INFOGEST 2.0 static *in vitro* simulation protocol. Interestingly, in different media (water, simulated gastric fluid, bicarbonate, and simulated intestinal fluid), the sodalite ZIF-8 topology in liposome-based lipid/ZIF-8 particles undergoes a crystalline phase transition to the denser, more stable ZIF-C phase. This transition, along with deeper internalization of astaxanthin in liposome-based particles, significantly influences the kinetics of release encapsulated astaxanthin. In summary, this study provides valuable insights into the synthesis of hybrid lipid/ZIF-8 biocomposites, the encapsulation of hydrophobic molecules, and the importance of crystalline phase transitions in MOFs within biological environments, highlighting their potential as drug delivery vehicles.

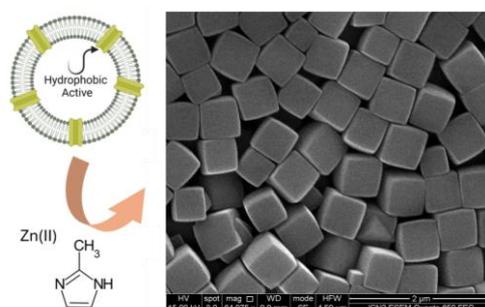


Figure 1. SEM image of Astaxanthin loaded liposome/ZIF-8 nanoparticles.

### References

[1] Cano-Sarabia, M.; Aydin, F.; Meng, L.; Gil-Bonillo, M.; Fonseca, J.; Dietrich, M.; Renner, S.; Amenitsch, H.; Falcaro, P.; Imaz, I.; MasPOCH, D. Lipid/ZIF-8 Biocomposites Based on Liposomes or Vesicles: In Situ Formation, and Preliminary Evaluation as Delivery Vehicles for Hydrophobic Drugs. *Small* **2025**, 2407051.

## Controlled Growth of PCN-224 on Plasmonic Nanoparticles: Engineering Photoactive Microporous Nanocarriers

Manuel CEBALLOS<sup>1</sup>, Sanuel FUNES-HERNANDO<sup>1</sup>, Giulia Zampini<sup>1</sup>, Manuela CEDRÚN-MORALES<sup>1</sup>, José Manuel VILA-FUNGUEIRIÑO<sup>1</sup>, Beatriz PELAZ<sup>1</sup> and Pablo DEL PINO<sup>1</sup>.

<sup>1</sup> Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CiQUS), Universidade de Santiago de Compostela, 15782 Santiago de Compostela, Spain  
E-mail: (manuel.ceballos.guzman@usc.es)

Metal-Organic Frameworks (MOFs) are crystalline, porous materials composed of metal or metal cluster nodes coordinated by polytopic organic ligands. Their unique physicochemical properties make them highly attractive for applications in gas storage and separation, catalysis, drug delivery, chemical sensing, and water treatment, among others.[1] Meanwhile, plasmonic nanoparticles exhibit exceptional optical properties due to the oscillation of conduction electrons upon excitation, a phenomenon known as Localized Surface Plasmon Resonance (LSPR). These properties make them valuable for applications in catalysis, sensing, and photothermal heating.[2,3]

This study presents the fabrication of microporous plasmonic nanocomposites (NCs) using gold nanobipyramids (AuB) as seeds to grow PCN-224 MOF shells of tunable thickness, ranging from 69 to 138 nm. The synthetic strategy is based on a pre-synthesized Zr<sub>6</sub>-oxo cluster and proceeds at room temperature. Notably, the concentration of AuB seeds directly influences both the yield of NCs and the resulting PCN-224 shell thickness, illustrating a seeded-growth mechanism. The thermoplasmonic response of these NCs is found to be strongly dependent on shell thickness, with thicker shells exhibiting enhanced thermal confinement properties.

As a proof of concept, the NCs are loaded with cresyl violet (CV), a lysosomal fluorescent marker, demonstrating thermoplasmonic-induced intracellular release upon near-infrared (NIR) photostimulation of the AuB's plasmonic band. Furthermore, the NCs exhibit remarkable photodynamic activity when excited at the PCN-224's Soret band. These findings highlight a facile, efficient, and reproducible methodology for fabricating NCs with controlled geometry while unlocking new opportunities in the field of nanoMOFs as multifunctional theranostic probes.[4]

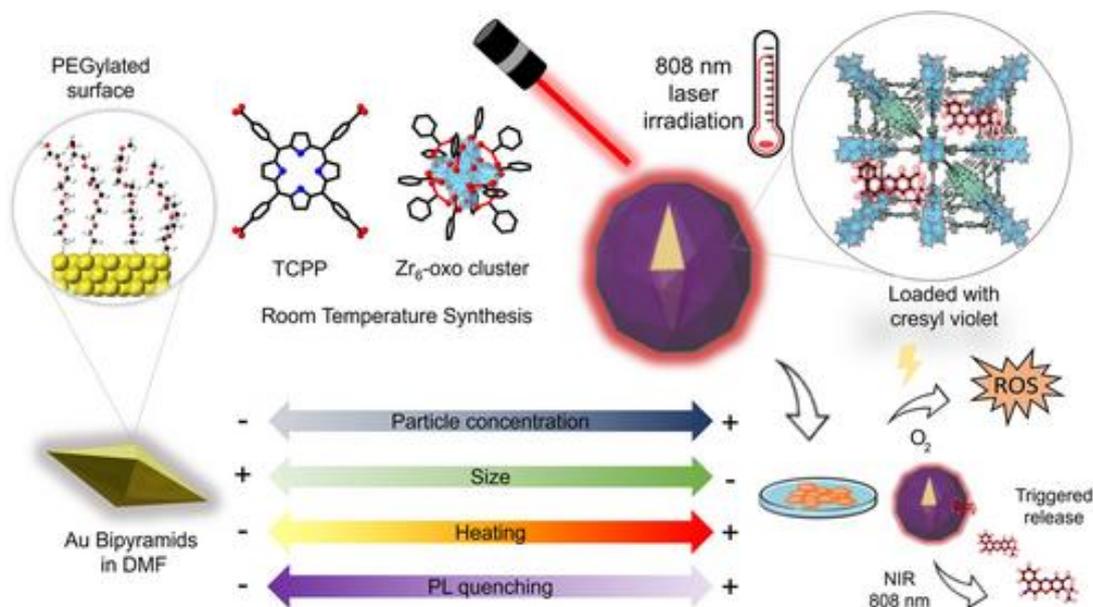


Figure 1. Scheme of the present work that provides a summary of the impact of AuB concentration on the size, heating efficiency, and luminescent properties of AuB@PCN-224 NCs.

## References

- [1] Ceballos, M.; Cedrún-Morales, M.; Rodríguez-Pérez, M.; Funes-Hernando, S.; Vila-Funqueiriño, J. M.; Zampini, G.; Navarro-Poupard, M. F.; Polo, E.; del Pino, P.; Pelaz, B. High-yield halide-assisted synthesis of metal–organic framework UiO-based nanocarriers. *Nanoscale*. **2022**, 14, 18, 6789-6801.
- [2] Carrillo-Carrión, C.; Martínez, R.; Polo, E.; Tomás-Gamasa, M.; Destito, P.; Ceballos, M.; Pelaz, B.; López, F.; Mascareñas, J. L.; del Pino, P. Plasmonic-assisted thermocyclizations in living cells using metal–organic framework based nanoreactors. *ACS Nano*. **2021**, 15, 10, 16924-16933.
- [3] Cedrún-Morales, M.; Ceballos, M.; Soprano, E.; Zampini, G.; Polo, E.; Pelaz, B.; del Pino, P. Light-Responsive Nanoantennas Integrated into Nanoscale Metal–Organic Frameworks for Photothermal Drug Delivery. *Small Science*, **2024**, 4, 8, 2400088.
- [4] Ceballos, M.; Funes-Hernando, S.; Zampini, G.; Cedrún-Morales, M.; Vila-Funqueiriño, J. M.; Pelaz, B.; del Pino, P. Seeded-Growth of PCN-224 onto Plasmonic Nanoparticles: Photoactive Microporous Nanocarriers. *Small Structures*. **2024**, 5, 5, 2300464.

## Metal–Organic Frameworks in (Bio)Sensing: Integrating Luciferases and Nanozymes for Robust Analytical Platforms

Héctor Martínez-Pérez-Cejuela<sup>1</sup>, Ernesto F. Simó-Alfonso<sup>1</sup>, José M. Herrero-Martínez<sup>1</sup>, Maria Maddalena Calabretta<sup>2</sup>, Elisa Michelini<sup>2</sup>

<sup>1</sup> Department of Analytical Chemistry, Faculty of Chemistry, University of Valencia, Dr. Moliner 50, Burjassot 46100, Spain

<sup>2</sup> Department of Chemistry “Giacomo Ciamician”, Alma Mater Studiorum—University of Bologna, Via Piero Gobetti 85, I-40129 Bologna, Italy

E-mail: Hector.Martinez-Perez@uv.es

Metal–organic frameworks (MOFs) have emerged as a versatile class of porous crystalline materials with significant potential in biosensing applications, owing to their tunable porosity, chemical versatility, and structural stability. In recent years, the immobilization of biomolecules such as luciferases within MOF matrices has enabled the development of hybrid platforms that combine the high sensitivity of bioluminescent detection with the physical robustness of MOFs. Specifically, the incorporation of thermostable luciferase mutants into ZIF-8 has resulted in enhanced catalytic performance, improved tolerance to pH and temperature fluctuations, and increased storage stability—even under ambient conditions—when compared to free enzymes [1]. These biocomposites have shown excellent results in real-sample analysis for ATP detection, achieving femtomolar detection limits using simple, portable devices such as smartphones and silicon photomultipliers [2].

Parallel to this, MOFs are also being engineered as enzyme mimics or nanozymes, mimicking peroxidase-like activity for applications where biological components are undesirable due to their fragility or cost. These synthetic analogues offer key advantages: they are not constrained by the cold-chain logistics that limit enzyme-based systems, exhibit superior thermal and chemical stability, and can be mass-produced reproducibly. However, despite their robustness, nanozymes often lack the catalytic specificity and efficiency of natural enzymes, potentially affecting the selectivity in complex biological matrices [3].

This dual approach—biomolecule-MOF hybrids for high-specificity biosensing and enzyme-free MOF nanozymes for rugged field applications—illustrates the expanding toolkit MOFs provide for next-generation analytical platforms. The challenges ahead include improving the catalytic activity of nanozymes to rival natural enzymes, optimizing MOF synthesis for scale-up, and ensuring the biocompatibility and environmental safety of MOF-based devices.

### References

- [1] Martínez-Pérez-Cejuela, H., Gregucci, D., Calabretta, M. M., Simó-Alfonso, E. F., Herrero-Martínez, J. M., Michelini, E. Novel Nanozeolitic Imidazolate Framework (ZIF-8)–Luciferase Biocomposite for Nanosensing Applications. *Anal. Chem.*, **2022**, 95, 4, 2540–2547.
- [2] Martínez-Pérez-Cejuela, H., Calabretta, M. M., Bocci, V., D’Elia, M., Michelini, E. Super-Stable Metal–Organic Framework (MOF)/Luciferase Paper-Sensing Platform for Rapid ATP Detection. *Biosensors*, **2023**, 13, 4, 451.
- [3] Martínez-Pérez-Cejuela, H., Calabretta, M. M., Michelini, E. Chemiluminescence “Add-and-Measure” Sensing Paper Based on the Prussian Blue/Metal–Organic Framework MIL-101 Nanozyme for Rapid Hydrogen Peroxide Detection. *Anal. Chem.* **2024**, 96, 42, 16561–16569.

### Acknowledgments

This study was funded by grants PID2021-125459OB-I00 funded by MCIN/AEI/10.13039/501100011033 and by “ERDF A way of making Europe.”

## Surface Functionalization of Zirconium-Based MOFs with Phosphate-Containing Bioactive Molecules for Targeted Cellular Interactions

Giulia ZAMPINI<sup>1</sup>, Manuel CEBALLOS<sup>1</sup>, Samuel FUNES-HERNANDO<sup>1</sup>, Beatriz PELAZ<sup>1</sup>, Pablo DEL PINO<sup>1</sup>

<sup>1</sup> CiQUS, Universidade de Santiago de Compostela, 15782 Santiago de Compostela, Spain.

E-mail: giulia.zampini@usc.es

Surface functionalization of Metal-Organic Frameworks (MOFs) is essential for modifying their chemophysical properties, which directly affect interactions with biological systems [1]. In biomedical applications, these modifications play a key role in determining how nanoscale MOFs (NMOFs) interact with cells, influencing internalization, metabolism, and cellular responses. Each functionalization strategy fine-tunes NMOFs for specific biomedical applications and targeting mechanisms [2].

In this study, PCN-224 was synthesized with a diameter below 100 nm and functionalized with biologically relevant molecules [1] bearing phosphate groups. In fact, a promising strategy for the rapid and efficient chemisorption of bioactive molecules is to leverage the strong affinity of zirconium-based MOFs (Zr-MOFs) for phosphate groups, which leads to the Zr-O-P bond formation [3].

Fructose-functionalized NMOFs were designed to target cancer cells with elevated fructose metabolism, potentially enhancing therapeutic delivery. Glucose-functionalized NMOFs aimed to exploit increased glucose uptake in cancer cells, improving drug delivery efficiency. Mannose-functionalized NMOFs were developed to target macrophages and immune cells, modulating immune responses and inflammation. Additionally, adenosine-di/tri-phosphate (ADP/ATP)-functionalized NMOFs were explored due to their role in cellular energy metabolism and signaling, potentially influencing cell proliferation, apoptosis, and drug resistance mechanisms in targeted therapy.

The optical and colloidal properties of functionalized MOFs were fully characterized, confirming effective modification. Cell viability assay, using A549 as cell model, revealed variable toxicity levels at 200 ppm of Zr depending on the type of functionalization, indicating different degree of interaction NMOFs-cells and, possibly, different particles internalization. These findings underscore the tunability of PCN-224 NMOFs in modulating cellular interactions, paving the way for their application in precision nanomedicine.

### References

- [1] Chen, X.; Mercado Argandona, S.; Melle, F.; Rampal, N.; Fairen-Jimenez, D. Advances in surface functionalization of next-generation metal-organic frameworks for biomedical applications: Design, strategies, and prospects. *Chem* **2024**, 10, 2, 504-543.
- [2] Yang, J.; Yang, Y-W. Metal-Organic Frameworks for Biomedical Applications. *Small* **2020**, 16, 10, 1906846.
- [3] Chen, X.; Zhuang, Y.; Rampal, N.; Hewitt, R.; Divitini, G.; O'Keefe, C. A.; Liu, X. Formulation of Metal-Organic Framework-Based Drug Carriers by Controlled Coordination of Methoxy PEG Phosphate: Boosting Colloidal Stability and Redispersibility. *J. Am. Chem. Soc.* **2021**, 143, 34, 13557-13572.

## Surface Functionality in NanoCOFs Drives Enhanced Cellular Uptake in Lung Cancer Cells

Sumanta CHOWDHURY<sup>1</sup>, Preeti RATHI<sup>2</sup>, Prem FELIX SIRIL\*<sup>1</sup>

<sup>1</sup> Indian Institution of Technology Mandi, School of Chemical Sciences, Kamand-175005, India

<sup>2</sup> Indian Institution of Technology Mandi, School of Biosciences and Bioengineering, Kamand-175005, India

E-mail: [d18002@students.iitmandi.ac.in](mailto:d18002@students.iitmandi.ac.in), [sumanta.chowdhury@univ-nantes.fr](mailto:sumanta.chowdhury@univ-nantes.fr)

While conventional research on covalent organic frameworks (COFs) has prioritized their drug-loading capacity and controlled release for drug delivery nanoplatforms, their structure-property-cellular internalization mechanisms remain underexplored.<sup>[1]</sup> In this study, we demonstrate that subtle functional group variations in nanoCOFs critically govern their surface chemistry and subsequent cellular uptake behavior. To isolate functionality as the sole variable, we synthesized biocompatible imine-linked isoreticular nanoCOFs with identical backbones, uniform particle sizes (75–80 nm), and consistent spherical morphologies. Additionally, surface modification with *Pluronic-F127* ensured enhanced colloidal stability in cell culture and phosphate buffer saline media over extended periods. The conjugation of Cyanine-5 dye with nanoCOFs enabled the visualization of cellular internalization using confocal laser scanning microscopy. The findings demonstrated notable variations in the internalization efficiency of nanoCOFs in A549 lung cancer cells, which could be directly linked to their surface chemistry. Hence, this study opens up possibilities for designing COF-based nanocarriers with tailored functionalities to achieve tunable cellular uptake for precise chemotherapeutic applications.

### References

[1] Singh, N.; Son, S.; An, J.; Kim, I.; Choi, M.; Kong, N.; Tao, W.; Kim, J. S. Nanoscale Porous Organic Polymers for Drug Delivery and Advanced Cancer Theranostics. *Chem. Soc. Rev.* **2021**, *50* (23), 12883–12896.

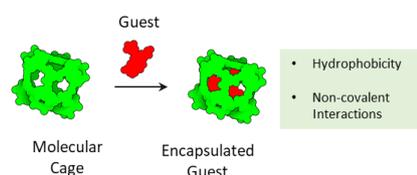
## Tailoring Molecular Cages for Guest Binding, Sensing, and Biomedical Applications

Vicente Martí-Centelles,<sup>a,b,c</sup> Giovanni Montà-González,<sup>a,c</sup> Eduardo Ortiz-Gómez,<sup>a,c</sup> Rocío López-Lima,<sup>a,c</sup> Guillermo Fiorini,<sup>a,c</sup> Guillermo Hernández-Sigüenza,<sup>a</sup> David Bastante Rodríguez,<sup>a,d</sup> Eva Garrido,<sup>a,b</sup> Alba García-Fernández,<sup>a,b,d</sup> Paula M. Soriano-Teruel,<sup>a,c,e</sup> Alfredo López Olvera,<sup>a</sup> Ramón Martínez-Mañez<sup>a,b,c,d,e</sup>

<sup>a</sup>Instituto Interuniversitario de Investigación de Reconocimiento Molecular y Desarrollo Tecnológico (IDM), Universitat Politècnica de València, Universitat de València, Camino de Vera s/n, 46022, Valencia, Spain. <sup>b</sup>CIBER de Bioingeniería Biomateriales y Nanomedicina, Instituto de Salud Carlos III, Spain. <sup>c</sup>Unidad Mixta de Investigación en Nanomedicina y Sensores, Universitat Politècnica de València, Instituto de Investigación Sanitaria La Fe (IISLAFE), Avenida Fernando Abril Martorell, 106, 46026, Valencia, Spain. <sup>d</sup>Unidad Mixta UPV-CIPF de Investigación en Mecanismos de Enfermedades y Nanomedicina, Valencia, Universitat Politècnica de València, Centro de Investigación Príncipe Felipe, Avenida Eduardo Primo Yúfera, 3, 46012, Valencia, Spain. <sup>e</sup> Departamento de Química, Universitat Politècnica de València, Camí de Vera s/n, 46022, Valencia, Spain.

E-mail: [vimarcel@upv.es](mailto:vimarcel@upv.es)

Supramolecular chemists have developed a toolbox of methods that allow preparing molecular cages with cavities with customized sizes and properties, for guest encapsulation with applications in catalysis, molecular recognition, sensing, catalysis, and emerging biomedical applications.<sup>[1-2]</sup> In general, cage synthesis involves the self-assembly of building blocks with precise shape and geometry under equilibrium control to yield the most stable cage structure.<sup>[3]</sup> The cage structure can be designed using molecular modelling to obtain any desired cavity size and shape with specific functional groups pointing towards the cavity.<sup>[4]</sup> This communication will show how to determine the cavity volume and hydrophobicity and ESP using CageCavityCalc,<sup>[4]</sup> and different synthetic strategies to obtain molecular cages from different building blocks to obtain porous organic cages and porous metal-organic cages.<sup>[5,6]</sup> The host-guest properties of the cages towards different guests, including anticancer drugs, will be presented (Figure 1).



**Figure 1.** Scheme showing the encapsulation of a guest molecule by a molecular cage.

**Acknowledgements:** V.M.-C. acknowledges the financial support from projects ESGENT/2024/001 and CIDEGENT/2020/031 both funded by the Generalitat Valenciana, Project PID2020-113256RA-I00 funded by MICIU/AEI/10.13039/501100011033, and Project CNS2023-144879 funded by MICIU/AEI/10.13039/501100011033 and European Union NextGenerationEU/PRTR. R.M.-M. acknowledges the financial support from Project PROMETEO CIPROM/2021/007 from the Generalitat Valenciana and project PID2021-126304OB-C41 funded by MICIU/AEI/10.13039/501100011033/ and FEDER A way to make Europe. This research was supported by CIBER - Consorcio Centro de Investigación Biomédica en Red- (CB06/01/2012), Instituto de Salud Carlos III, Ministerio de Ciencia e Innovación. E.O.-G. is grateful to the GVA for Grisolia grant (CIGRIS/2021/128). R.L.-L. is grateful to the GVA for Grisolia grant (CIGRIS/2022/123). G.F. is grateful to the GVA for ACIF grant (CIACIF/2022/112). D.B.-R. is grateful to the GVA for ACIF grant (CIACIF/2022/174). G.H. is grateful to the Spanish Ministerio de Universidades for her FPU grant (FPU21/04727). E.G. is grateful to the Spanish MIU and European Union-Next Regeneration EU for her “Margarita Salas” postdoctoral grant (UP2021-036). P.M.S.-T. is grateful to the Generalitat Valenciana for a postdoctoral Investigo contract (INVEST/2023/443). E.C. thanks the Instituto de Salud Carlos III (Miguel Servet 2023 CP23/00086). A.L.O. is grateful to the EU for MSCA-PF fellowship (GA:101146953).

**References:** [1] G. Montà-González, E. Ortiz-Gómez, R. López-Lima, G. Fiorini, R. Martínez-Mañez, V. Martí-Centelles, *Molecules* **2024**, *29*, 1621. [2] G. Montà-González, F. Sancenón, R. Martínez-Mañez, V. Martí-Centelles, *Chem. Rev.* **2022**, *122*, 13636. [3] V. Martí-Centelles, *Tetrahedron Lett.* **2022**, *93*, 153676. [4] V. Martí-Centelles, T. K. Piskorz, F. Duarte. *J. Chem. Inf. Model.* **2024**, *64*, 5604. [5] G. Montà-González, Martínez-Mañez, V. Martí-Centelles, *Targets* **2024**, *2*, 372. [6] G. Montà-González, D. Bastante-Rodríguez, A. Garcia-Fernandez, P. Lusby, R. Martínez-Mañez, V. Martí Centelles, *Chem. Sci.* **2024**, *15*, 10010.

## Sepiolite as a porous nanocarrier to enhance mirtazapine drug delivery

Ana BORREGO-SÁNCHEZ<sup>1</sup>, Miquel MARTÍNEZ-NAVARRETE<sup>1</sup>, J. Alejandro BERNABEU-MARTÍNEZ<sup>1</sup>, Xuefan CHEN<sup>1</sup>, Antonio J. GUILLOT<sup>1</sup>, Ana MELERO<sup>1</sup>

<sup>1</sup> *Department of Pharmacy and Pharmaceutical Technology and Parasitology, University of Valencia, 46100 Valencia, Spain*  
E-mail: ana.maria.borrego@uv.es

Clay minerals are porous materials with nanometric internal spaces that facilitate the adsorption and desorption of water molecules and other compounds. Among them, sepiolite stands out due to its long channels, which can adsorb drugs, acting as a pharmaceutical excipient, capable of interacting with active ingredients to modify their delivery [1]. These properties make the sepiolite a promising nanocarrier for the design of novel release systems of drugs, such as mirtazapine. Mirtazapine is an antidepressant drug. It is administered orally, requiring high doses to overcome its low solubility and bioavailability. The dissolution of the drug is the limiting factor for absorption in the gastrointestinal tract [2]. Improving its dissolution could enable lower oral doses and potentially reduce side effects.

In this study, a combination of theoretical and experimental approaches was employed to evaluate the effectiveness of sepiolite as a nanocarrier for mirtazapine delivery.

Theoretical calculations were performed with LAMMPS program [3], and CVFF force field [4]. Experimentally, the mirtazapine-sepiolite interaction product was prepared by dissolving the drug in absolute ethanol and bringing it into contact with the clay for a sufficient period to ensure adsorption equilibrium. Then, the solvent was evaporated, and the resulting mirtazapine-sepiolite product was characterized by X-ray Powder Diffraction, Differential Scanning Calorimetry, Thermogravimetric Analysis and Fourier Transform Infrared Spectroscopy. In vitro dissolution tests were also conducted to evaluate the improvement in the drug dissolution profiles.

The computational study results confirmed the possibility of adsorption of mirtazapine in the sepiolite channels, revealing atomistic-level interactions. Experimentally, it was also demonstrated that the drug was effectively intercalated in sepiolite channels by using a non-aqueous polar medium (ethanol), thereby overcoming the solubility limitations common in aqueous systems for poorly water-soluble drugs. The mirtazapine-sepiolite interaction product increased the dissolution rate of drug, showing an immediate release. This interaction product can be considered as a promising alternative for improving the oral bioavailability of mirtazapine.

### References

- [1] García-Villén, F; Carazo, E; Borrego-Sánchez, A; Sánchez-Espejo, R; Cerezo, P; Viseras, C; Aguzzi, C. Chapter 6 - Clay minerals in drug delivery systems. *Modified Clay and Zeolite Nanocomposite Materials, Micro and Nano Technologies*. **2019**, 129–166.
- [2] Davis, M.P. Mirtazapine and Depressions. *NeuroPsychopharmacotherapy*. **2020**, 1–29.
- [3] Plimpton, S. Fast parallel algorithms for short-range molecular dynamics. *J. Comput. Phys.* **1995**, 117,1–19.
- [4] Heinz, H; Lin, TJ; Kishore Mishra, R; Emami, FS. Thermodynamically consistent force fields for the assembly of inorganic, organic, and biological nanostructures: the INTERFACE force field. *Langmuir*. **2013**, 29, 1754–1765.

## Bio-Metal-Organic Frameworks for the Removal of Emergent Contaminants

Jesús Ferrando Soria<sup>1</sup>, Thais Grancha,<sup>1</sup> Emilio Pardo<sup>1</sup>, Donatella Armentano<sup>2</sup>, Sergio Armenta<sup>3</sup>, José Manuel Herrero-Martínez<sup>3</sup>

<sup>1</sup> Instituto de Ciencia Molecular (ICMol), Valencia, Spain

<sup>2</sup> Università della Calabria, Cosenza, Italy

<sup>3</sup> Departamento de Química Analítica, Universitat de València, c/Dr. Moliner, 50, 46100 Burjassot, Valencia, Spain  
E-mail: [jesus.ferrando@uv.es](mailto:jesus.ferrando@uv.es)

Water contamination is one of the main environmental issues mankind is nowadays facing and directly threatens the planet's environmental balance and sustainability of life on Earth for future generations. The development of novel and efficient methods for water remediation is a pressing need.<sup>1</sup> Metal-Organic Frameworks (MOFs), have strongly burst into the environmental remediation scenario.<sup>2</sup> This in part is consequence of the unique intrinsic features of MOFs. Taking advantage of them, we have developed a family of robust and water-stable MOFs as efficient adsorbents of inorganic and organic contaminants commonly found in wastewater.<sup>3</sup> However, we realized this is just a preliminary-step to solve the decontamination of aquatic ecosystems. Thus, we need to move forward and structure the best performing MOFs into materials able to be implemented in current decontamination protocols.<sup>4</sup>

In this context, firstly, I will show you the most remarkable results we have achieved on the removal of emergent contaminants from water, making a special emphasis of how attractive is to take advantage of the modular nature of Multivariate-MOF (MTV-MOFs).<sup>3</sup> Then, I will present our investigations on the structuration of the best performing materials in the form of extruded pellets, mixed-matrix membranes (MMMs) and single-walled carbon nanotube bucky papers (SWCNTs-BP).<sup>3,4</sup> Remarkably, the results presented in this contribution evidence the viability of integrate (MTV)-MOFs on different supports, while retaining their removal efficiency, and more importantly evidence the game-changer character of MOFs in real-life, which apart of showing potential to solve existing environmental issues, reunite the required characteristics to be adapted in decontamination protocols

### References

- [1] (a) United Nations, Transforming our world: the 2030 Agenda for Sustainable Development, <https://sustainabledevelopment.un.org/post2015/transformingourworld>. (b) US EPA, *Drinking Water Requirements for States and Public Water Systems 2018 Edition of the Drinking Water Standards and Health Advisories Tables (EPA 822-F-18-001)*, **2018**.
- [2] (a) M. Mon, R. Bruno, J. Ferrando-Soria, D. Armentano and E. Pardo, *J. Mater. Chem. A* **2018**, 6, 4912-4947. (b) S. Rojas and P. Horcajada, *Chem. Rev.* **2020**, 120, 8378-8415.
- [3] (a) C. Negro, H. Martínez Pérez Cejuela, E. F. Simó-Alfonso, J. M. Herrero-Martínez, R. Bruno, D. Armentano, J. Ferrando-Soria and E. Pardo, *ACS Appl. Mater. Interfaces* **2021**, 13, 28424-28432.
- [4] (a) M. Baratta, T. F. Mastropietro, R. Bruno, A. Tursi, C. Negro, J. Ferrando-Soria, A. I. Mashin, A. Nezhdanov, F. Nicoletta, G. De Filipo, E. Pardo, D. Armentano, *ACS Appl. Nano Mater.* **2022**, 5, 5223-5233. (c) C. Negro, H. Martínez Pérez Cejuela, E. F. Simó-Alfonso, W. Iqbal, J. M. Herrero-Martínez, D. Armentano, J. Ferrando-Soria and E. Pardo, *ACS Appl. Mater. Interfaces* **2023**, 15, 3069-3076.

## New synthetic strategies to access chemically diverse MOF biocomposites

Jesús CASES DÍAZ<sup>1</sup>, Mónica GIMÉNEZ MARQUÉS<sup>1</sup>

<sup>1</sup> *Universitat de València, Instituto de Ciencia Molecular, Catedrático José Beltrán Martínez 2, Paterna, Spain*

E-mail: [jesus.cases@uv.es](mailto:jesus.cases@uv.es)

The encapsulation of biomolecules in solid supports is essential to provide stability against harsh environmental conditions, a requisite towards their exploitation in pharmaceutical and biotechnological fields.

Metal-Organic Frameworks (MOFs) have emerged as promising supports for biomolecule immobilization due to their physicochemical stability, tunable properties (such as particle size, pore size, and hydrophobicity), and controlled biodegradability. Their modular nature also enables biocompatible synthesis conditions, such as the in-situ synthesis, wherein MOFs spontaneously assemble around biomolecules<sup>1</sup>. Leveraging this principle, we recently demonstrated that employing hard Lewis acid cations as MOF precursors enables efficient encapsulation across various protein types, leading to optimized MIL-100(Fe) biocomposites<sup>2</sup>.

In this case, the strategy has been explored with synthetically challenging MOFs, such as HKUST-1. We present an alternative method for synthesizing protein@HKUST-1 composites using protein@Cu-BTC dense composites as precursors<sup>3</sup>. This process involves a pH-dependent in situ formation and their subsequent transformation into HKUST-1. The resulting solid support protects proteins from denaturation by organic solvents and proteolytic agents. Also, reversible transformation from a dense to a porous structure enables fine-tuning of encapsulated cytochrome C (CytC) activity, achieving a 4-fold increase by modulating mass transport across the support.

Additionally, polyols, are commonly employed as cryoprotectant and/or osmolytes in the preparation of proteins stock solutions for long term storage. These compounds, including ethylene glycol (EG), propylene glycol (PG) and glycerol (Gly), when employed as co-solvents, increase stability and prevent aggregation of proteins. Direct synthesis of HKUST-1 and protein@HKUST-1 composites employing polyols as cosolvents is evaluated.

### References

1. Liang, K. *et al.* Biomimetic mineralization of metal-organic frameworks as protective coatings for biomacromolecules. *Nat. Commun.* **6**, 7240 (2015).
2. Cases Díaz, J., Lozano-Torres, B. & Giménez-Marqués, M. Boosting Protein Encapsulation through Lewis-Acid-Mediated Metal–Organic Framework Mineralization: Toward Effective Intracellular Delivery. *Chem. Mater.* (2022) doi:10.1021/acs.chemmater.2c01338.
3. Díaz, J. C. & Giménez-Marqués, M. Alternative protein encapsulation with MOFs: overcoming the elusive mineralization of HKUST-1 in water. *Chem. Commun.* **60**, 51–54 (2024).

## OnG7: A Metal–Organic Framework for Potential Chemotherapeutic Delivery in Breast Cancer Treatment

Darragh MCHUGH<sup>1</sup>, Sha LI<sup>2</sup>, Róisín M. DWYER<sup>2</sup> and Constantina PAPATRIANTAFYLLOPOULOU<sup>1</sup>

<sup>1</sup> School of Biological and Chemical Sciences, College of Science and Engineering, University of Galway, H91 TK33 Galway, Ireland.

<sup>2</sup> School of Medicine, Lambe Institute for Translational Research, University of Galway, Galway, Ireland

E-mail: d.mchugh13@universityofgalway.ie

While cancer treatments continue to evolve, metastatic and surgery-resistant cancers—such as triple-negative breast cancer (TNBC)—remain among the most challenging to treat, with limited therapeutic options and poor prognoses. Enhancing drug bioavailability in tumours while minimising off-target toxicity is critical for improving treatment outcomes. In recent years, metal–organic frameworks (MOFs) have emerged as promising nanocarriers due to their high drug-loading capacity, biocompatibility, and tuneable properties. [1-4]

Here, we present OnG7 (where OnG stands for Ollscoil na Gaillimhe (University of Galway)), a novel porous MOF designed for drug encapsulation and controlled release. Constructed from a zinc-oxo cluster and an elongated multitopic carboxylate linker, OnG7 exhibits a mesoporous architecture with a surface area of approximately 5000 m<sup>2</sup>/g and pore size of 2.2 nm. Dynamic light scattering and zeta potential analysis revealed nanoparticle sizes of 310.4 ± 18 nm with a surface charge of -12 ± 0.1 mV under physiological conditions.

Following the high loading of doxorubicin (49.6 ± 1.2 wt %) and paclitaxel (36.1 ± 1.5 wt %), OnG7 formulations were assessed for colloidal stability and biocompatibility. In vitro studies on two TNBC cell lines demonstrated efficient cellular internalisation, low cytotoxicity in drug-free formulations, and sustained drug release. Notably, investigations using a 3D breast cancer spheroid model revealed pH-responsive drug release within the hypoxic core, mimicking in vivo tumour microenvironments. [5]

These findings support OnG7's potential as a promising drug delivery platform, addressing key challenges in chemotherapy by improving therapeutic precision in aggressive and hard-to-treat cancers.

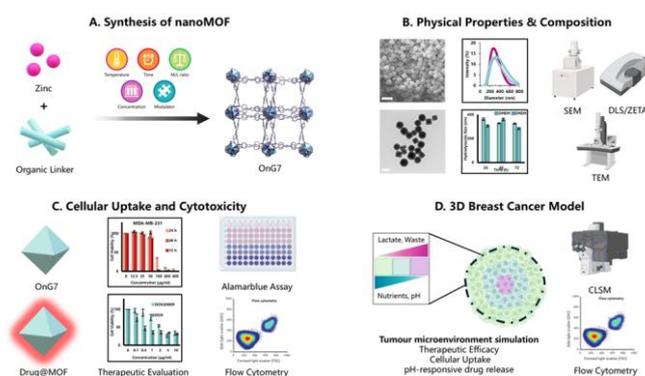


Figure 1 Synthesis, Characterisation, and Biological Assessment of OnG7 for Breast Cancer Therapy

### References

[1] Howard, F. M.; Olopade, O. I. Epidemiology of Triple-Negative Breast Cancer: A Review. *Cancer J.* **2021**, *27*, 8–16.

[2] Melle, F.; Menon, D.; Connot, J.; Ostolaza-Paraiso, J.; Mercado, S.; Oliveira, J.; Chen, X.; Mendes, B. B.; Conde, J.; Fairen-Jimenez, D. Rational Design of Metal–Organic Frameworks for

Pancreatic Cancer Therapy: From Machine Learning Screening to In Vivo Efficacy. *Adv. Mater.* **2025**, *241*, 2757.

[3] Forgan, R. S. Reproducibility in Research into Metal–Organic Frameworks in Nanomedicine. *Commun. Mater.* **2024**, *5*, 46.

[4] Ahmed, A.; McHugh, D.; Papatriantafyllopoulou, C. Synthesis and Biomedical Applications of Highly Porous Metal–Organic Frameworks. *Molecules* **2022**, *27*, 6585.

[5] Tchoryk, A.; Taresco, V.; Argent, R. H.; Ashford, M.; Gellert, P. R.; Stolnik, S.; Grabowska, A.; Garnett, M. C. Penetration and Uptake of Nanoparticles in 3D Tumor Spheroids. *Bioconjugate Chem.* **2019**, *30*, 1371–1384.

## Supramolecular Strategies for Guest Encapsulation and Release at the Molecular Scale

Rocío López-Lima<sup>1</sup>, Félix Sancenón-Galarza<sup>1,2,3,4,5</sup>, Ramón Martínez-Máñez<sup>1,2,3,4,5</sup>, Vicente Martí-Centelles<sup>1,2,3</sup>

<sup>1</sup>Instituto Interuniversitario de Investigación de Reconocimiento Molecular y Desarrollo Tecnológico (IDM), Universitat Politècnica de València, Universitat de València, Camino de Vera s/n, 46022 Valencia, Spain. <sup>2</sup>Departamento de Química, Universitat Politècnica de València, Camno de Vera s/n, 46022 Valencia, Spain. <sup>3</sup>CIBER de Bioingeniería Biomateriales y Nanomedicina, Instituto de Salud Carlos III, 46022 Valencia, Spain. <sup>4</sup>Unidad Mixta de Investigación en Nanomedicina y Sensores, Instituto de Investigación Sanitaria La Fe (IISLAFE), Universitat Politècnica de València, Avenida Fernando Abril Martorell, 106, 46026 Valencia, Spain <sup>5</sup>Unidad Mixta UPV-CIPF de Investigación en Mecanismos de Enfermedades y Nanomedicina, Centro de Investigación Príncipe Felipe, Universitat Politècnica de València, Avenida Eduardo Primo Yúfera, 3, 46012 Valencia, Spain.

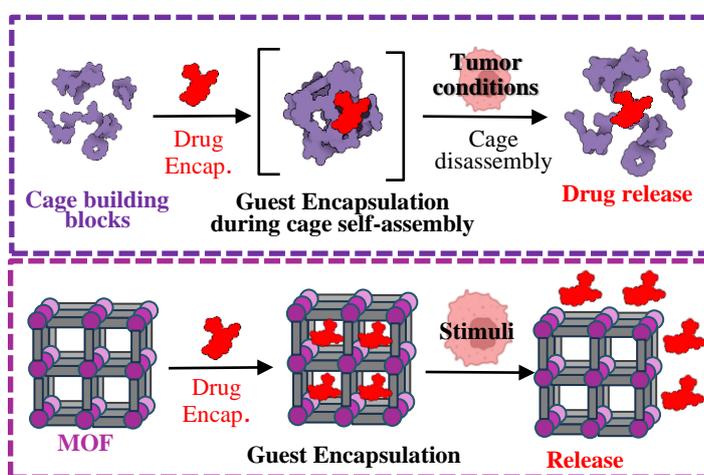
[rloplim@doctor.upv.es](mailto:rloplim@doctor.upv.es)

Molecular cages are synthetic host systems with diverse applications in catalysis, sensing, and molecular recognition. Owing to their unique structural and functional properties, they have attracted considerable interest in biological applications; however, their advancement in this field remains in its early stages [1–3]. Comparable characteristics can be observed in metal-organic frameworks (MOFs) [4], which also provide porous architectures with potential for a wide range of functional applications. Our research focuses on the design of molecular cages for the encapsulation of anticancer drugs, facilitating their controlled release in response to specific stimuli. In this approach, therapeutic agents are confined within the cavity of the cages, which subsequently undergo disassembly under tumour-specific intracellular or microenvironmental conditions, leading to the targeted release of the encapsulated payload. A similar level of control can be achieved using MOFs, which enable precise drug delivery. In this study, we present the design and synthesis of various molecular systems and their encapsulation and release efficiency.

**Acknowledgements:** V.M.-C. acknowledges the financial support from projects ESGENT/2024/001 and CIDEGENT/2020/031 funded by the Generalitat Valenciana, Project PID2020-113256RA-I00 funded by MICIU/AEI/10.13039/501100011033, and Project CNS2023-144879 funded by MICIU/AEI/10.13039/501100011033 and European Union NextGenerationEU/PRTR. R.M.-M. acknowledges the financial support from Project PROMETEO CIPROM/2021/007 from the Generalitat Valenciana and project PID2021-126304OB-C41 funded by MICIU/AEI/10.13039/501100011033/ and FEDER A way to make Europe. This research was supported by CIBER (CB06/01/2012), Instituto de Salud Carlos III, Ministerio de Ciencia e Innovación. R.L.-L. is grateful to the GVA for Grisolia grant (CIGRIS/2022/123).

### References

- [1] Montà-González, G.; Ortiz-Gómez, E.; López-Lima, R.; Fiorini G.; Martínez-Máñez, R.; Martí-Centelles, V. Water-Soluble Molecular Cages for Biological Applications. *Molecules*, **2024**, *29*, 1621.
- [2] Montà-González, G.; Bastante-Rodríguez, D.; García-Fernández, A.; Lusby, P.; Martínez-Máñez, R.; Martí-Centelles, V. Comparing organic and metallo-organic hydrazone molecular cages as potential carriers for doxorubicin delivery. *Chem. Sci.* **2024**, *15*, 1001.
- [3] Montà-González, G.; Sancenón, F.; Martínez-Máñez, R.; Martí-Centelles, V. Purely Covalent Molecular Cages and Containers for Guest Encapsulation. *Chem. Rev.* **2022**, *122*, 13636.



**Figure 1.** Scheme showing the encapsulation and release of a guest molecule by a molecular cage (top) and a MOF (bottom).

## Atrane-Based Synthesis of Potencial Theranostic Mesoporous Silica Materials for MRI and XFCT Imaging

M. Dolores GARRIDO<sup>1</sup>, José Francisco SERRANO-CLAUMARCHIRANT<sup>2</sup>, Bejan HAMAWANDI<sup>2</sup>, Jamal EL HASKOURI<sup>1</sup>, José Vicente ROS-LIS<sup>3</sup>, Pedro AMORÓS<sup>1</sup>, Muhammet S. TOPRAK<sup>2</sup>

<sup>1</sup> Institut de Ciència dels Materials (ICMUV), Universitat de València, Catedrático José Beltrán 2, 46980 Paterna, Valencia, Spain.

<sup>2</sup> KTH Royal Institute of Technology, Department of Applied Physics, SE106 91 Stockholm, Sweden

<sup>3</sup> Instituto Interuniversitario de Investigación de Reconocimiento Molecular y Desarrollo Tecnológico (IDM), Universitat de València, Dr. Moliner 50, 46100 Burjassot, Valencia, Spain  
maria.d.garrido@uv.es

Nanoparticles have been engineered as biomedical materials for various purposes, including bio-imaging and drug delivery, a combination referred to as theranostics. Mesoporous silica stands out as a highly promising carrier due to its inherent biocompatibility and the ability of its porous architecture to encapsulate pharmaceutically active compounds. This study presents various potential theranostic agents designed for magnetic resonance imaging (MRI) and X-ray fluorescence computed tomography (XFCT) applications. These materials were synthesized using the atrane method [1], which enables the homogeneous and well-dispersed incorporation of heteroelements. Additionally, the water solubility of the atrane complex ensures a uniform synthesis medium, facilitating the formation of highly homogeneous coatings. Two distinct materials were developed for MRI applications. The first consists of a UVM-7 silica in which gadolinium has been incorporated to function as a T2 contrast agent [2]. The second involves a core-shell architecture, where the core comprises a cluster of superparamagnetic iron oxide nanoparticles (SPIONs) synthesized via microwave-assisted methods. This core is subsequently coated within a mesoporous silica shell, where a fluorescent molecule's loading and release dynamics have been systematically investigated [3]. The first material of the XFCT contrast agents is a europium-doped UVM-7 mesoporous silica, whose pores had been loaded with a ruthenium complex. Europium was chosen for its phosphorescent properties, while ruthenium was selected due to its X-ray fluorescence characteristics and potential anticancer activity. The final material follows a core-shell design, where the core consists of molybdenum dioxide (MoO<sub>2</sub>), which is subsequently coated with mesoporous silica. All the materials presented in this work exhibit significant potential for theranostic applications as they integrate contrast-enhancing elements with mesoporous silica architectures capable of encapsulating therapeutic agents, enabling their controlled release under specific conditions.

### References

[1] Garrido, M.D.; Benítez, M.; Ros-Lis, J.V.; Amorós, P. A travel through the atrane route, a versatile tool for the materials soft-synthesis: A twenty-five years perspective. *Nano Select*, **2024**, *5*, 2300169.

[2] Garrido, M.D.; Puchol, N.; El Haskouri, J.; Sánchez-Royo, J.F.; Folgado, J.V.; Gonzalez Marrachelli, V.; Pérez Terol, I.; Ros-Lis, J.V.; Marcos, M.D.; Ruíz, R.; Beltrán, A.; Morales, J.M.; Amorós, P. High content and dispersion of Gd in bimodal porous silica: T2 contrast agents under ultra-high magnetic fields. *Microporous Mesoporous Mater.*, **2022**, *336*, 111863.

[3] Garrido, M.D.; Hamawandi, B.; Serrano-Claumarchirant, J.F.; Saladino, G.M.; Ergül, A.B.; Marcos, M.D.; Ros-Lis, J.V.; Amorós, P.; Toprak, M.S. A rapid synthesis of magnetic-core mesoporous silica-shell nanostructures—as potential theranostic agents—by means of microwave irradiation and the atrane method, *Nanoscale*, **2025**, *17*, 6539-6549.

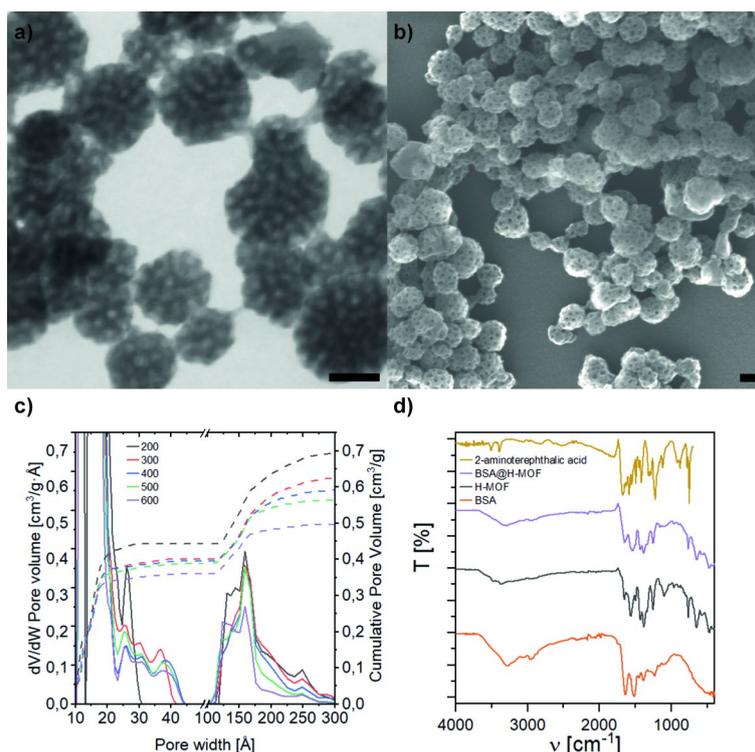
## Protein adsorption and thermal protection within the mesopores of a nano-Hierarchical-MOF (H-UiO-66-NH<sub>2</sub>)

Samuel Funes-Hernando<sup>1</sup>, Manuel Ceballos<sup>1</sup>, Beatriz Pelaz<sup>1</sup> and Pablo del Pino<sup>1</sup>

<sup>1</sup> Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CiQUS),  
Universidade de Santiago de Compostela, 15705, España.

E-mail: samuel.funes.hernando@usc.es

Hierarchical Metal-Organic Frameworks (H-MOFs) feature multi-level porosity, from micro to macropores, enhancing adsorption, transport, catalysis, and drug delivery, among others. Their synthesis has rapidly evolved, with templating emerging as a promising method due to its control over surface areas, pore volumes, and sizes. [1] In our approach, toluene micelles dispersed in an aqueous solution, guided by the ClO<sub>4</sub><sup>-</sup> ion and stabilized by Pluronic block copolymer F127, direct UiO-66-NH<sub>2</sub> assembly. Upon reaction completion, H-MOFs form with pore sizes dictated by micelle size. [2] By varying acetic acid volume, we obtained H-MOFs (50–150 nm) with the typical UiO-66-NH<sub>2</sub> micropores and ~15 nm mesopores. These larger pores enable protein encapsulation, potentially protecting them from denaturation due to MOF thermal stability. As a proof of concept, BSA was encapsulated and characterized via DSC, FTIR, and SAXS, yielding promising results for both encapsulation and thermal protection.



**a, b)** scale bars in STEM and SEM images represent 50 nm, **c)** pore size distribution of the H-MOFs varying volume of acetic acid and **d)** FTIR in which the H-MOF has the amine peaks and the BSA@H-MOF doesn't have them.

### References

- [1]. Yao, Y., Zhao, X., Chang, G., Yang, X. & Chen, B. Hierarchically Porous Metal–Organic Frameworks: Synthetic Strategies and Applications. *Small Struct.* **4**, (2023).
- [2]. Li, K., Zhao, Y., Yang, J. & Gu, J. Nanoemulsion-directed growth of MOFs with versatile architectures for the heterogeneous regeneration of coenzymes. *Nat. Commun.* **13**, (2022).

## Ultraflexible Liposomal Nanoplatfoms for Vitamin B12 Delivery in Advanced Skin Disease Therapies

Miquel MARTÍNEZ-NAVARRETE<sup>1</sup>, Alejandro BERNABEU<sup>1</sup>, Antonio José GUILLOT<sup>1</sup>, Ana BORREGO-SÁNCHEZ<sup>1</sup>, Xuefan CHEN<sup>1</sup> Ana MELRO<sup>1</sup>

<sup>1</sup> *Universitat de València, Department of Pharmacy and Pharmaceutical Technology, Av Vicente Andrés Estellés sn 46100 Burjassot, Spain.  
E-mail: miquel.martinez-navarrete@uv.es*

Atopic dermatitis (AD) is a chronic inflammatory skin disease that affects approximately 10% of the global population at some point in their lives. Conventional treatments, such as topical corticosteroids and oral immunosuppressants, present significant limitations, including long-term side effects and limited efficacy in severe cases. This study proposes an alternative therapeutic strategy based on the topical administration of ultraflexible lipid vesicles encapsulating Cyanocobalamin (B12), a well-known antioxidant.

Ultraflexible lipid vesicles containing B12 (T-B12) were synthesized using the Bangham method. The resulting nanovesicles were sonicated, filtered, and extruded to reduce their size and enhance their homogeneity. The formulation showed optimal characteristics for topical delivery, including particle size <300 nm ( $132 \pm 1$  nm), low polydispersity index (< 0.3), and suitable zeta potential [1].

The efficacy of these formulations was evaluated *in vivo* using murine models of acute and chronic dermatitis. In the acute contact dermatitis model induced by TPA, mice treated with T-B12 exhibited a significant reduction in bioluminescence—used as a proxy for myeloperoxidase activity in inflamed tissues—comparable to that observed in corticosteroid-treated animals. In the chronic dermatitis model induced by repeated oxazolone (OXA) exposure, mice displayed typical symptoms such as flaking, irritation, and ear swelling. Treatment with T-B12 significantly reduced ear thickness and lowered levels of proinflammatory cytokines (IL-4, IL-1 $\beta$ , and TNF $\alpha$ ) compared to untreated controls.

These findings suggest that ultraflexible lipid vesicles offer a promising topical drug delivery platform for AD, potentially providing an effective and less invasive alternative to current therapies. The combined topical administration of B12 and CsA may represent a novel therapeutic approach with fewer systemic side effects.

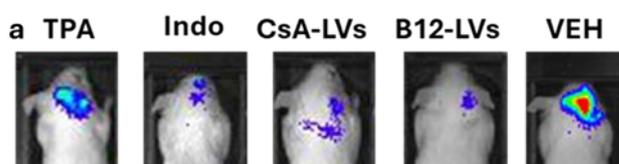


Figure 1: Bioluminescence induced by skin inflammation on ear mice under different conditions

### References

[1] Guillot AJ, Jornet-Mollá E, Landsberg N, Milián-Guimerá C, Montesinos MC, Garrigues TM, et al. Cyanocobalamin Ultraflexible Lipid Vesicles: Characterization And In Vitro Evaluation Of Drug-Skin Depth Profiles. *Pharmaceutics*. 2021, 13, 3, 418-440.

## Molecular Insights into Cyclosporine Adsorption on Montmorillonite: A Computational Approach

Xuefan CHEN<sup>1</sup>, Miquel MARTÍNEZ-NAVARRETE<sup>1</sup>, Alejandro J. BERNABEU<sup>1</sup>, Antonio J. GUILLOT<sup>1</sup>, Ana MELERO<sup>1</sup>, Ana BORREGO-SÁNCHEZ<sup>1</sup>

<sup>1</sup> Department of Pharmacy and Pharmaceutical Technology and Parasitology, University of Valencia, 46100 Valencia, Spain  
E-mail: xuechen@alumni.uv.es

Cyclosporine is a commonly prescribed immunosuppressant for the treatment of organ transplant rejection and severe active rheumatoid arthritis, among other pathologies [1]. However, its use is limited by its low bioavailability and significant side effects, mainly due to its poor aqueous solubility and high molecular weight [2]. Montmorillonite is a natural clay and a porous material with a unique nanoscale structure, featuring accessible internal spaces that facilitate adsorption-desorption phenomena [3]. These structural characteristics make it an effective pharmaceutical excipient for modifying drug solubility, release and bioavailability [4].

This study aimed to design montmorillonite-based delivery systems for improving cyclosporine bioavailability. As a first step, computational methods were used to study this system at the atomistic level.

In particular, LAMMPS program [5] and the CVFF Interface force field [6] were employed to investigate the molecular interactions between cyclosporine and montmorillonite.

The simulations enabled the study of the cyclosporine-montmorillonite adsorption complex, revealing the main molecular interactions between the drug and the clay. Moreover, the simulations provided valuable information regarding the expansion of the clay's interlayer space and its drug loading capacity.

Computational calculations are useful for designing clay-based drug delivery systems and suggest that montmorillonite could be a suitable carrier to improve cyclosporine bioavailability, which may lead to reduced dosing requirements and minimized adverse effects.

### References

- [1] Pradier, A.; Papaserafeim, M.; Li, N.; et al. Small-Molecule Immunosuppressive Drugs and Therapeutic Immunoglobulins Differentially Inhibit NK Cell Effector Functions in Vitro. *Front. Immunol.* **2019**, 10, 556.
- [2] Chiu, Y.; Higaki, K.; Neudeck, B.; et al. Human Jejunal Permeability of Cyclosporin A: Influence of Surfactants on P-glycoprotein Efflux in Caco-2 Cells. *Pharm. Res.* **2003**, 20, 5, 749–756.
- [3] Bergaya, F.; Lagaly, G. General Introduction: Clays, Clay Minerals, and Clay Science. *Dev. Clay Sci.* **2006**, 1, 1–18.
- [4] Viseras, C.; Cerezo, P.; Sánchez, R.; Salcedo, I.; Aguzzi, C. Current Challenges in Clay Minerals for Drug Delivery. *Appl. Clay Sci.* **2010**, 48, 291–295.
- [5] Plimpton, S. Fast Parallel Algorithms for Short-range Molecular Dynamics. *J. Comput. Phys.* **1995**, 117, 1, 1-19.
- [6] Heinz, H.; Lin, T.; Mishra, R.; Emami, F. Thermodynamically Consistent Force Fields for the Assembly of Inorganic, Organic, and Biological Nanostructures: The INTERFACE Force Field. *Langmuir.* **2013**, 29, 6, 1754-1765.

## Synthesis of highly crystalline imine-based COF nanospheres with tunable sizes

Nikolaos Liodakis,<sup>a</sup> Manuel Ceballos, Beatriz Pelaz<sup>a</sup> and Pablo del Pino<sup>a</sup>

<sup>a</sup>Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CiQUS)

E-mail: niliodakis@gmail.com

Covalent Organic Frameworks (COFs) are crystalline, porous materials composed primarily of light elements, resulting in low-density materials with large surface area. Each monomer within a COF, referred to as a Building Block (BB), offers a vast array of possibilities for creating à la carte COF materials with diverse properties and topologies. Notably, COFs exhibit exceptional resistance to both thermal and chemical treatments, enhancing their robustness.<sup>[1]</sup>

This study focuses on the synthesis of COF nanospheres for biological applications. The selected imine-linked triazine COFs, composed of 2,4,6-triphenyl-1,3,5-triazine (TTA), 2,7-Diaminofluorene (DAF) and p-Phenylenediamine (PDA) with benzene-1,3,5-tricarbaldehyde (TFB). These COFs demonstrate high crystallinity, porosity, and remarkable resistance to both thermal and chemical treatments. The synthesized materials consist of highly monodispersed nanospheres with varying sizes ranging from 50 to 250 nm, depending on the synthetic conditions. While traditional COF synthesis requires multiple days<sup>[2]</sup>, this study successfully achieves a highly porous and crystalline COF in under 24 hours.

These fluorescent nanospheres (Figure 1), which require no additional dyes, are particularly well-suited for biological applications due to their high porosity and ability to integrate with inorganic nanoparticles, such as gold bipyramids and palladium cubes. Furthermore, their surface contains free amino groups, enabling functionalization with polyethylene glycol (PEG), which significantly enhances colloidal stability

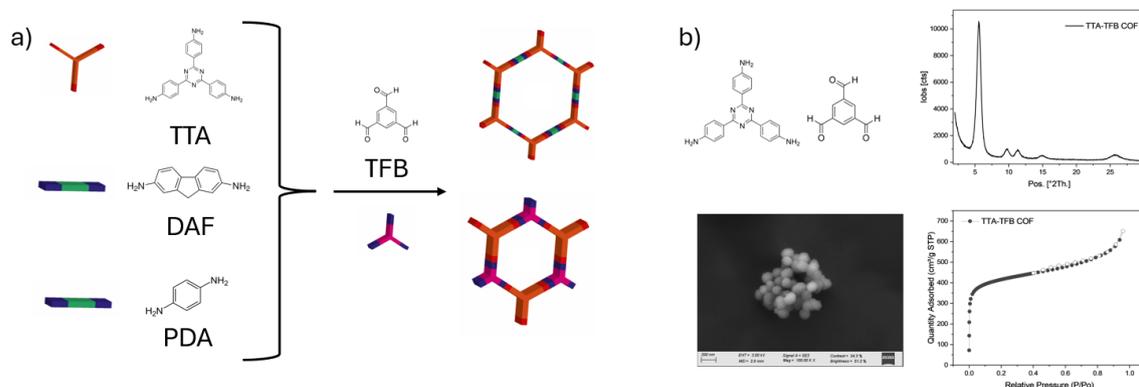


Figure 1. a) Scheme of the BBs and the Hexagonal structures, b) Characterization of the TTA-TFB COF, SEM image, PXRD pattern and BET surface area

[1] Syed Shoaib Ahmad Shah, Muhammad Sufyan Javed, Tayyaba Najam, *J. Materials Today* (2023), 67, 229-255

[2] Rodríguez-San-Miguel, D., Yazdi, A., Guillerm, V., Pérez-Carvajal, J., Puentes, V., MasPOCH, D., & Zamora, F. *Chemistry—A European Journal*, (2017), 23, 8623-8627.