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Functional framework materials for biomedical applications

Ross S. Forgan, *^a Ruxandra Gref *^b and Jianqiang Liu *^c

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The COVID-19 pandemic and subsequent global roll-out of vaccines based on the delivery of mRNA sequences formulated in lipid nanoparticles highlighted the vast potential of nanomedicine in tackling a range of

diseases and medical conditions.¹ Lipid nanoparticles are just one class of potential delivery vector, and so there are major ongoing research efforts investigating alternative materials to act as nanocarriers for a variety of active cargos, from small molecules to therapeutic proteins. In this regard, framework materials, such as metal–organic frameworks (MOFs), covalent organic frameworks (COFs), and hydrogen-bonded organic frameworks (HOFs), combine chemical and structural versatility to allow construction of highly functional porous materials. Consequently, research into

their biomedical application can be considered as still in an initial exponential growth phase.²

A wide range of framework materials, which show diversity in their dimensionality, chemical composition, crystallinity, and linkages (covalent, coordinative, and noncovalent), are available to researchers. Within the different sub-classes of framework materials, the ability to carefully select components with biocompatibility and functionality in mind means that materials can be tailored to a specific application, and they often exhibit multiplex functionality. For example,

^a School of Chemistry, University of Glasgow, Joseph Black Building, University Avenue, Glasgow G12 8QQ, UK. E-mail: ross.forgan@glasgow.ac.uk

^b Institut des Sciences Moléculaires d'Orsay, UMR 8216 CNRS, Paris Saclay University, France. E-mail: ruxandra.gref@universite-paris-saclay.fr

^c Guangdong Medical University, Dongguan, Guangdong 523000, China. E-mail: jianqiangliu8@gdmu.edu.cn



Ross S. Forgan

Prof. Ross S. Forgan is Professor of Supramolecular and Materials Chemistry at the University of Glasgow (UK). He obtained his PhD from the University of Edinburgh in 2008 and carried out postdoctoral research at Northwestern University (USA) and the University of Glasgow (UK). His group studies the modulated self-assembly of metal–organic frameworks, characterisation of key physical properties, and their application in drug delivery, catalysis, and sensing. He was awarded the Sessler Early Career Researcher Prize in 2018 and the RSC Bob Hay Lectureship in 2020, and is currently Chair of the RSC Porous Materials Interest Group.



Ruxandra Gref

Dr Ruxandra Gref is Research Director at the Institute of Molecular Sciences in Paris Saclay University (France). After a PhD thesis in the field of chemical engineering and polymer science, she carried out postdoctoral research at MIT, and obtained a permanent position at the National Research Center. Her group develops a platform of nanoparticles made of organic, inorganic and hybrid organic–inorganic materials to load a variety of drugs. The main applications include treating pulmonary infections (tuberculosis, COVID-19) and cancer, and elaborating devices to alleviate pain. She has more than 200 publications and 27 patents. She was awarded the silver medal of CNRS in 2019 and received the Trophée Star of Europe for coordinating a Marie Curie ITN network in 2018.

framework materials can act not only as drug carriers, but also have functionality embedded into their structures to allow concomitant imaging or novel therapeutic modalities, such as photodynamic and chemodynamic therapy. Their ability to go beyond being simple delivery vectors underpins much of the research into their bioapplications, and it is therefore not surprising that the first framework material to enter human trials is a Hf MOF for combined radiotherapy-radio-dynamic therapy (Phase I: NCT03444714; Phase II: NCT05838729), while a second is being assessed for synergic radiotherapy and immunotherapy (Phase I: NCT06182579). We have, therefore, curated this themed collection to highlight the diversity of structure, function, and application of framework materials in the hope of inspiring further ingenuity in their biomedical application.

The depth of the field is evident in the range of different framework materials discussed in this themed collection. Abánades Lázaro and Giménez-Marqués detail the synthesis of nanoscale MUV-2, a three-dimensional mesoporous Fe-MOF, which can load significant quantities of the anticancer chemotherapeutic paclitaxel and enhance the selectivity of its *in vitro* cytotoxicity (<https://doi.org/10.1039/D3TB01819A>). Liu and Wei detail two-dimensional Zn-MOF nanosheets containing ruthenium complexes, which can be hybridised with oligonucleotides to generate an electrochemical gene sensor (<https://doi.org/10.1039/D3TB01934A>). Furukawa *et al.* describe dirhodium metal-organic polyhedra (MOPs) –

discrete porous cage analogues of MOFs – which can be connected into amorphous coordination polymers that release NO from the porous cage of the MOP in response to light or water (<https://doi.org/10.1039/D3TB02162A>). Moving to organic systems, Zhao and Yan report an imine-linked COF containing porphyrin and anthracene moieties, which is capable of photogenerating (porphyrin) and storing (anthracene) $^1\text{O}_2$, and thus photosterilising wounds (<https://doi.org/10.1039/D3TB02017G>). Zhang, Kim and Song show that Ag_2O nanoparticles can be embedded within a microporous organic polymer to make processable coatings with excellent antibacterial properties (<https://doi.org/10.1039/D3TB02619A>). Finally, Yi and Wang describe encapsulation of charge-transfer co-crystals within the pores of a crystalline HOF, which exhibit significant absorption in the near infrared and so can be used for near-IR-II photothermal therapy against cancer both *in vitro* and *in vivo* (<https://doi.org/10.1039/D3TB01475D>). These examples underscore the wide functional toolkit available to materials scientists when tackling biological applications.

Perhaps as a consequence, this themed collection also covers a significant breadth of biological applications that go beyond conventional drug delivery. Rojas and Rodríguez-Diéguez review the latest advances in using MOFs and discrete metal complexes to both diagnose and treat Alzheimer's disease, representing a new frontier for MOF-based drug delivery and theranostics (<https://doi.org/10.1039/D3TB00427A>). Li

and Guo comprehensively review the application of magnetic two-dimensional nanocomposites against cancer, further expanding on the wide range of framework materials explored in this collection while also introducing exciting emerging technologies, including magnetic hyperthermia therapy, photothermal therapy, and photodynamic therapy (<https://doi.org/10.1039/D3TB02333H>). Wang reviews the use of MOFs and related hybrid materials as implantable devices, which may have applications in orthopaedics, cardiovascular disease, neural-tissue engineering, and general biochemical sensing *in situ* (<https://doi.org/10.1039/D3TB02620E>). Sensing is also the focus of a review by Kumar, Liu, Pan and Ouyang, who provide a comprehensive overview of the use of luminescent MOFs as probes for important biochemical analytes (<https://doi.org/10.1039/D3TB00505D>). Research articles also cover emerging applications. Yu describes the loading of Ga-MOFs with antimicrobial peptides to produce dual-mode antibacterial agents (<https://doi.org/10.1039/D3TB01754K>), complementing work by Mobin who loads Cu MOFs with isoniazid to inhibit bio-film formation (<https://doi.org/10.1039/D3TB02292G>). Lastly, Hao and Zhou show that dexamethasone-loaded ZIF-8 can be hybridised with wood aerogels, leading to bone regeneration at cranial defects in mouse models (<https://doi.org/10.1039/D3TB01484C>).

We hope that the themed collection provides a representative overview of the state-of-the-art framework materials and biomedical applications currently at the forefront of the field, serving both to highlight the huge potential of framework materials and inspire researchers towards the design of new materials and investigation of new applications.

References

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Jianqiang Liu

Jianqiang Liu obtained his PhD degree from Northwest University. Afterwards, he joined the School of Pharmacy at the Guangdong Medical University as an assistant professor in 2012. He was promoted to a full professor in 2018. From 2012 to 2019, he worked as a senior visiting scholar at Tsinghua University, and Yamagata University in Japan. His current research interest focuses on the development of functional materials including metal-organic frameworks (MOFs) and porous organic polymers (POPs) for energy, biology, and environment-related applications.