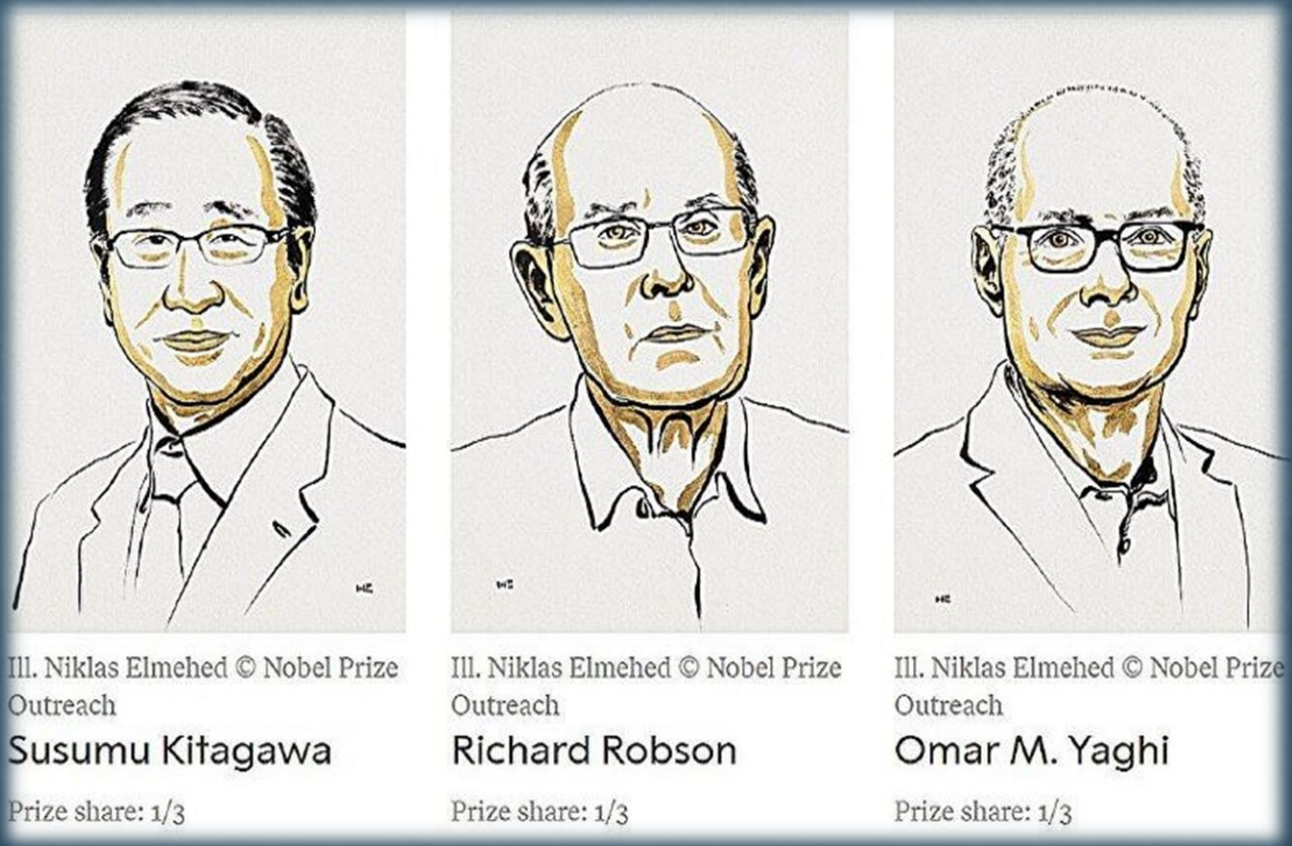
Three Minds, One Metal–Organic Frameworks: From Discovery to Application



By: Dr. Somaye Karimian

1404/07/28

Trends in Annual Publication of Metal–Organic Frameworks across Scientific Fields

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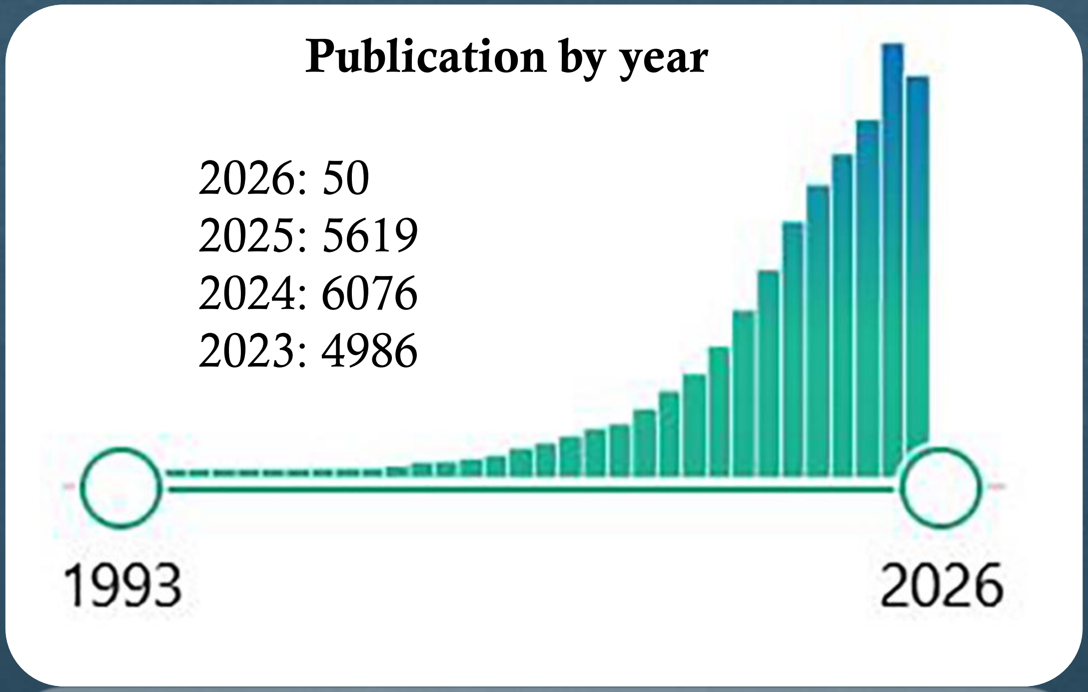
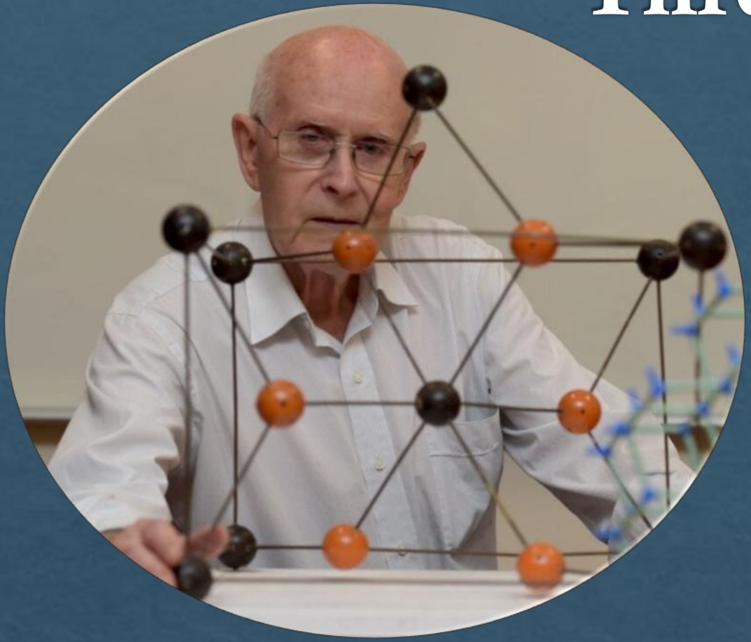


Three Minds that Shaped the Field



Richard Robson

4 June 1937, United Kingdom

University of Melbourne

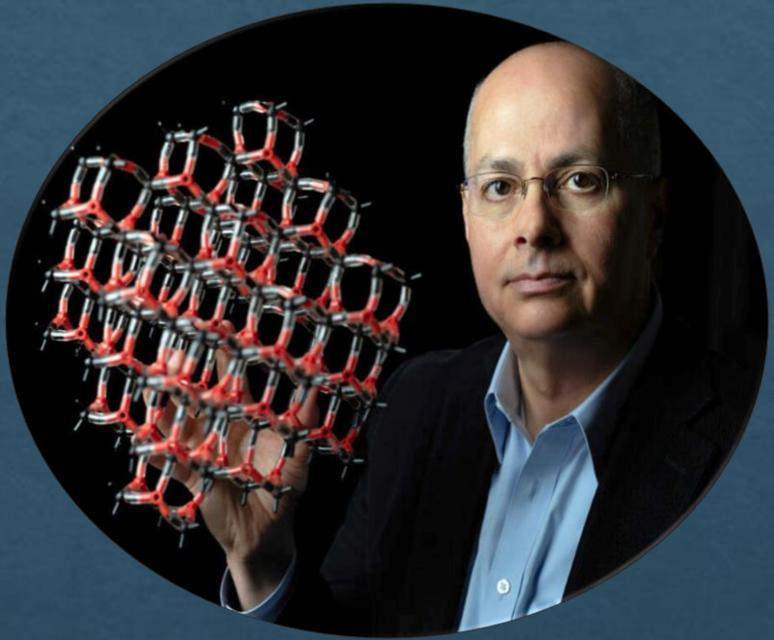
The Architect of Coordination Polymers

Susumu Kitagawa

4 July 1951, Kyoto, Japan

Kyoto University

The Master of Porous Frameworks



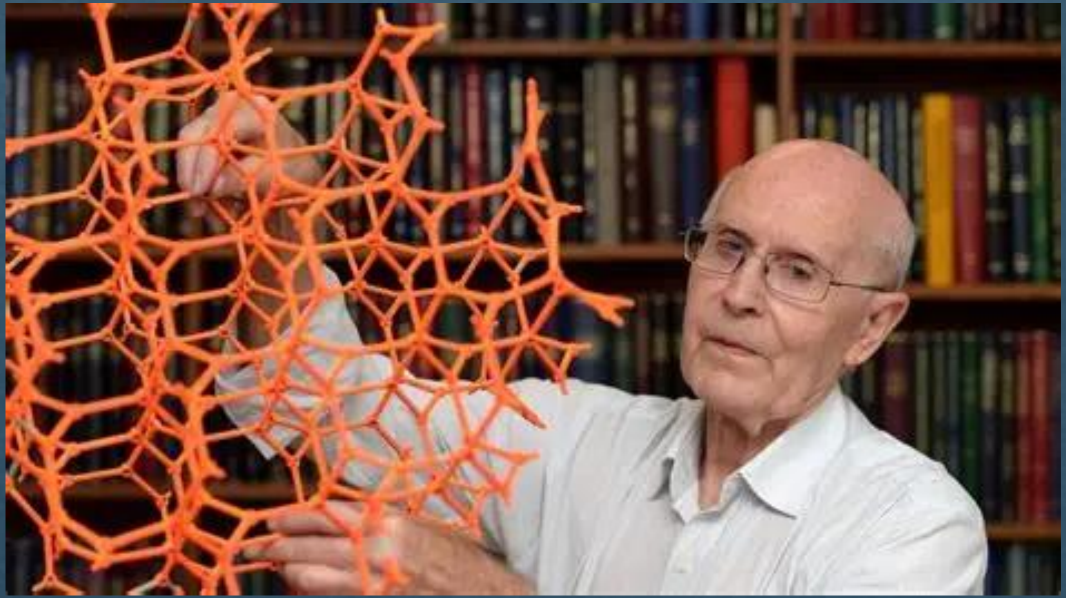
Omar Yaghi

9 February 1965, Amman

University of California, Berkeley

The Architect of Reticular Chemistry and secondary building units (SBUs)

Richard Robson



Robson, Richard

School of Chemistry, Melbourne, Australia • Scopus ID: 57206293562 • Connect to ORCID

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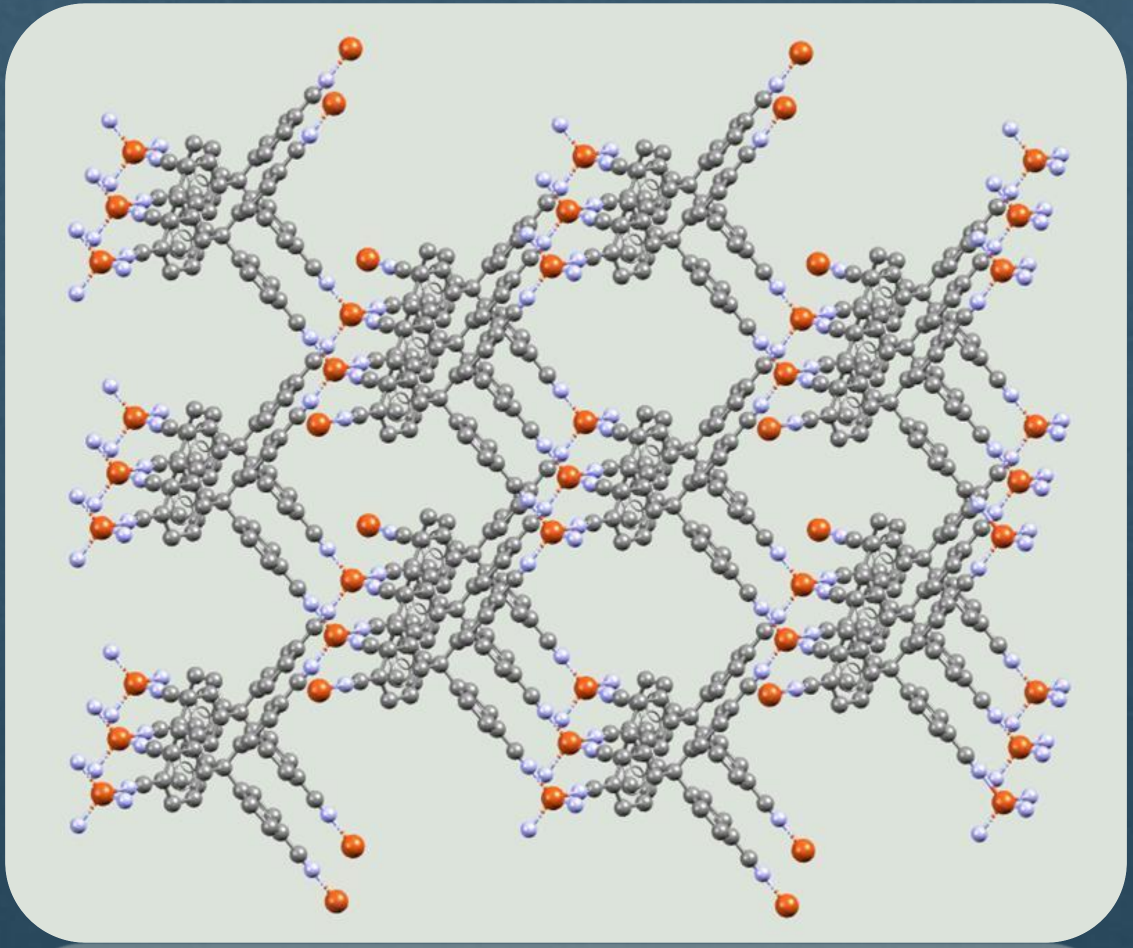
18,582	168	58
Citations by **12,402** documents	Documents	h-index

The 1989 coordination polymer that started it all was based on the structure of diamond



Susumu Kitagawa

“This is the mind of the researcher in Japan. Don’t switch off the light, even at night.”

Susumu **Kitagawa**

Current affiliation: Kyoto University, Kyoto, Japan

Scopus ID: 7201690696

88,165	814	140	6	1,383
Citations from **50,871** documents	Documents	*h*-index	Preprints	Co-authors

Google Scholar

Susumu Kitagawa

FOLLOW

Kyoto University

Verified email at icems.kyoto-u.ac.jp - Homepage

Chemistry of Coordination ... Porous Coordination Polym... Metal-Organic Frameworks

2025, Citations : 5042

TITLE	CITED BY	YEAR
Functional porous coordination polymers S Kitagawa, R Kitaura, S Noro Angewandte Chemie International Edition 43 (18), 2334-2375	12308	2004
Metal–organic frameworks (MOFs) S Kitagawa Chemical Society Reviews 43 (16), 5415-5418	4009	2014
Soft porous crystals S Horike, S Shimomura, S Kitagawa Nature chemistry 1 (9), 695-704	2497	2009
Terminology of metal–organic frameworks and coordination polymers (IUPAC Recommendations 2013) SR Batten, NR Champness, XM Chen, J Garcia-Martinez, S Kitagawa, ... De Gruyter	1716	2013
Highly controlled acetylene accommodation in a metal–organic microporous material R Matsuda, R Kitaura, S Kitagawa, Y Kubota, RV Belosludov, ... Nature 436 (7048), 238-241	1590	2005
Dynamic porous properties of coordination polymers inspired by hydrogen bonds S Kitagawa, K Uemura	1564	2005

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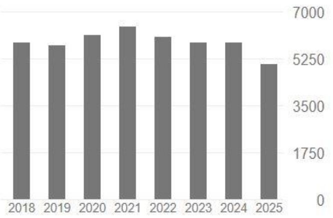

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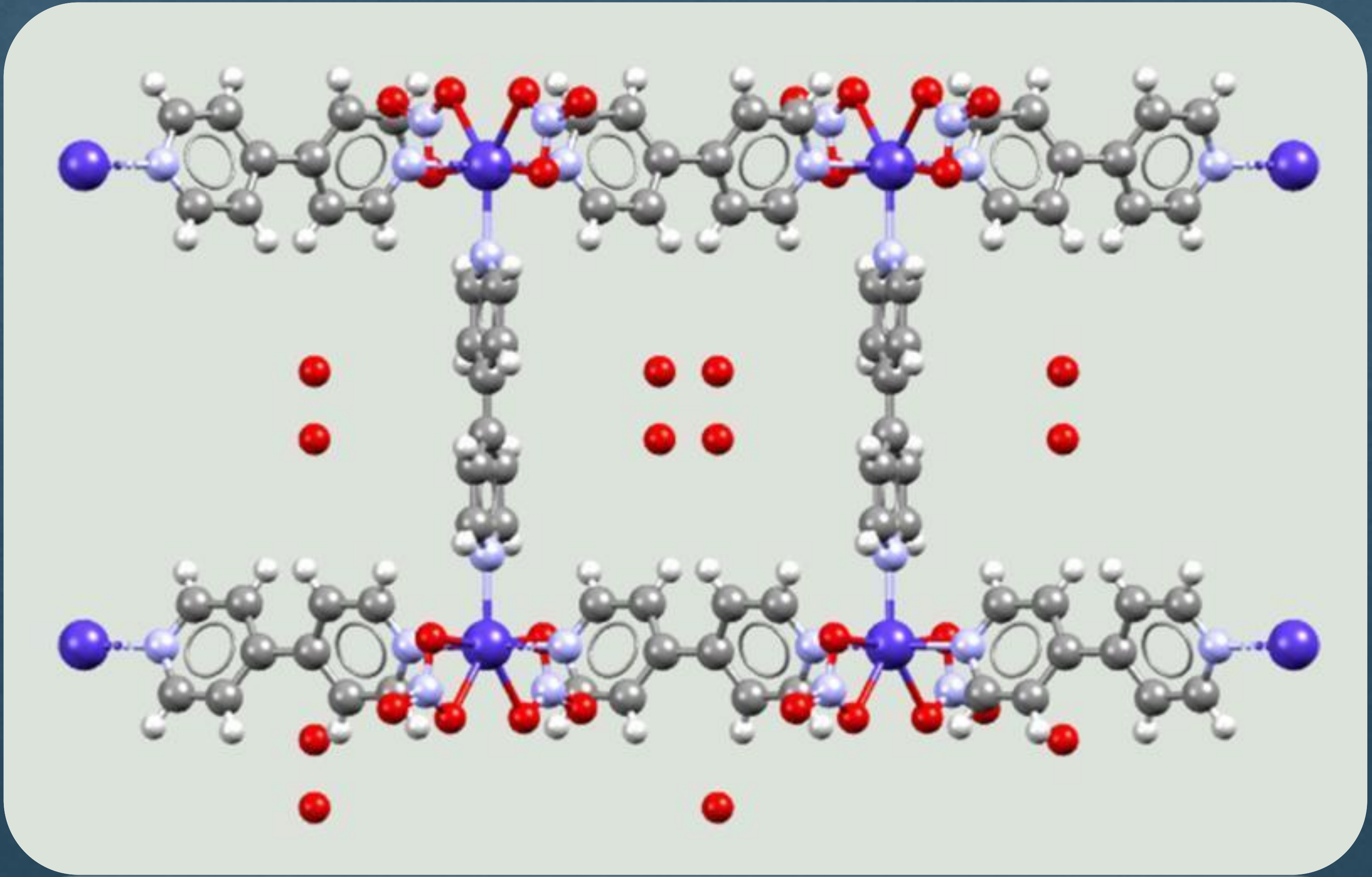
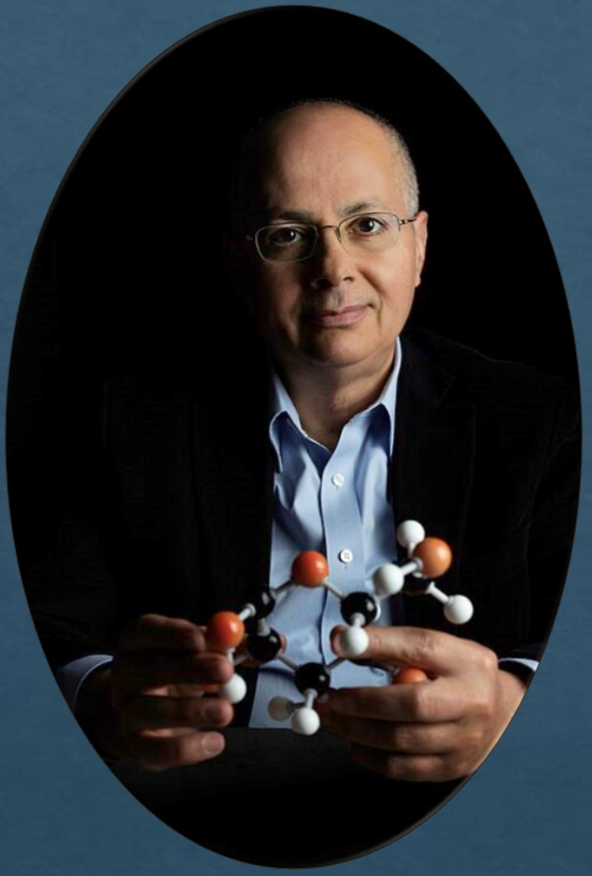
Kitagawa’s 1997 compound could absorb and release different gases from its pores



Omar M. Yaghi



Omar M. Yaghi

Current affiliation: Berkeley College of Chemistry, Berkeley, United States

Scopus ID: 7005061054

222,117	392	188	20	872
Citations from **96,850** documents	Documents	*h*-index	Preprints	Co-authors

Google Scholar

Omar M. Yaghi

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University Professor & James and Neeltje Tretter Professor of Chemistry, UC Berkeley
Verified email at berkeley.edu - Homepage

Reticular Chemistry Metal-Organic Framework Covalent Organic Framework

2025, Citations : 17999

TITLE	CITED BY	YEAR
The chemistry and applications of metal-organic frameworks H Furukawa, KE Cordova, M O'Keeffe, OM Yaghi Science 341 (6149), 1230444	16595	2013
Reticular synthesis and the design of new materials OM Yaghi, M O'Keeffe, NW Ockwig, HK Chae, M Eddaoudi, J Kim Nature 423 (6941), 705-714	10959	2003
Design and synthesis of an exceptionally stable and highly porous metal-organic framework H Li, M Eddaoudi, M O'Keeffe, OM Yaghi nature 402 (6759), 276-279	9954	1999
Systematic design of pore size and functionality in isoreticular MOFs and their application in methane storage M Eddaoudi, J Kim, N Rosi, D Vodak, J Wachter, M O'Keeffe, OM Yaghi Science 295 (5554), 469-472	9499	2002
Porous, crystalline, covalent organic frameworks AP Côté, AI Benin, NW Ockwig, M O'Keeffe, AJ Matzger, OM Yaghi science 310 (5751), 1166-1170	8072	2005
Exceptional chemical and thermal stability of zeolitic imidazolate frameworks	7933	2006

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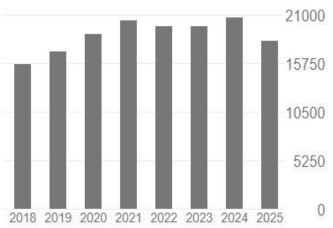
	All	Since 2020
Citations	274859	117751
h-index	197	147
i10-index	427	352



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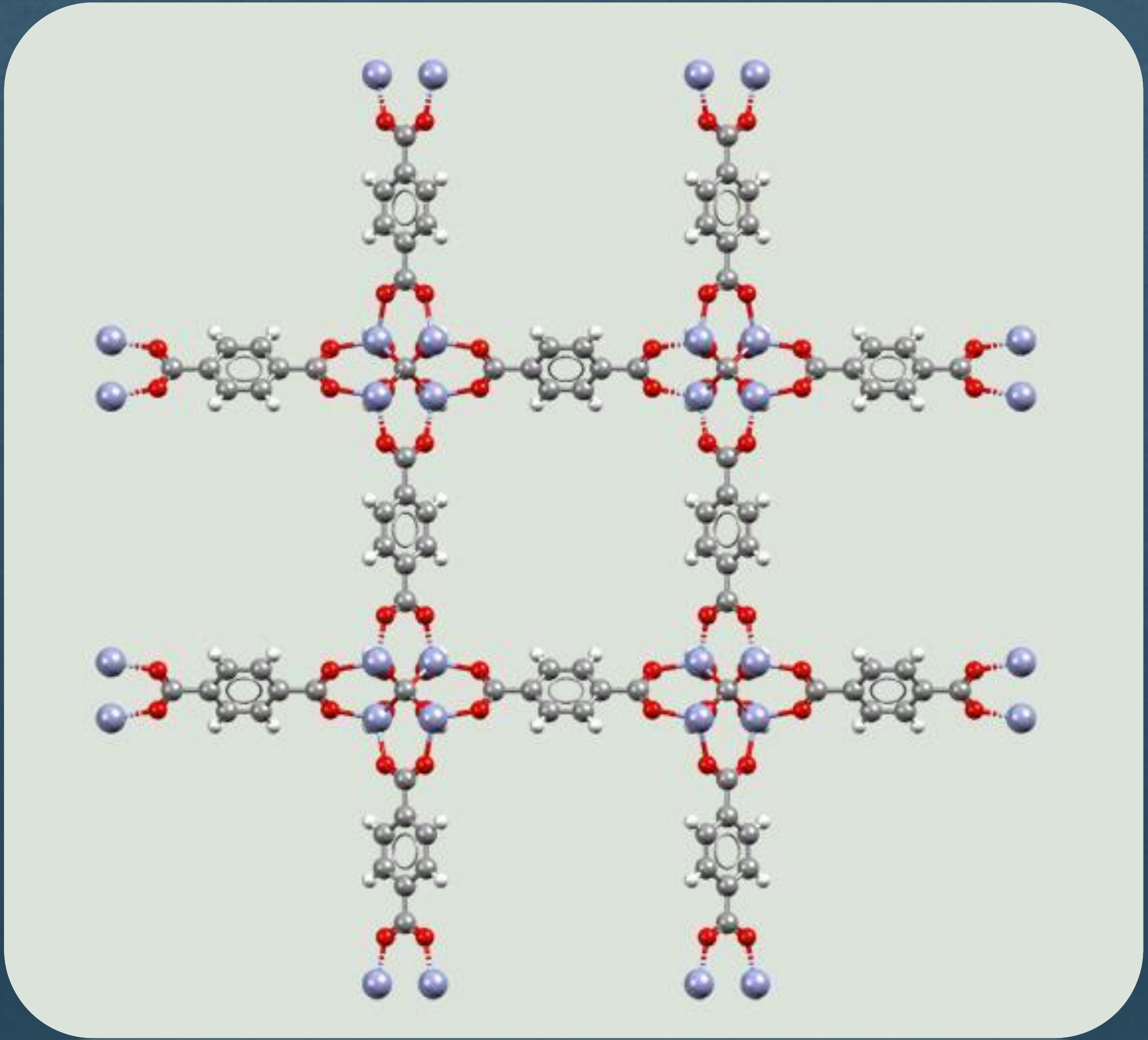
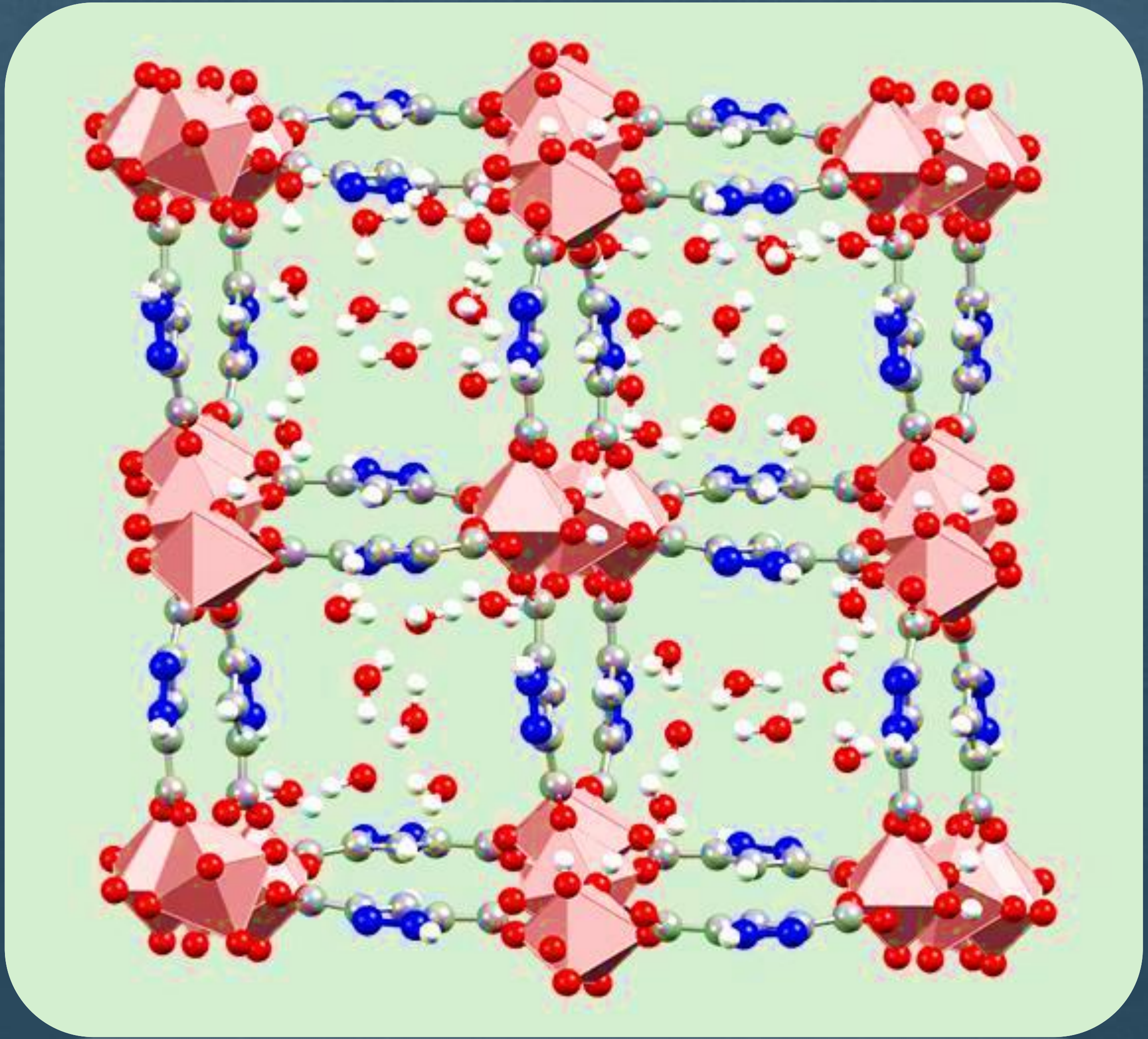
MOF-5 had incredible stability and porosity (1995)



A MOF-303 from 2021 can harvest water from dry desert air

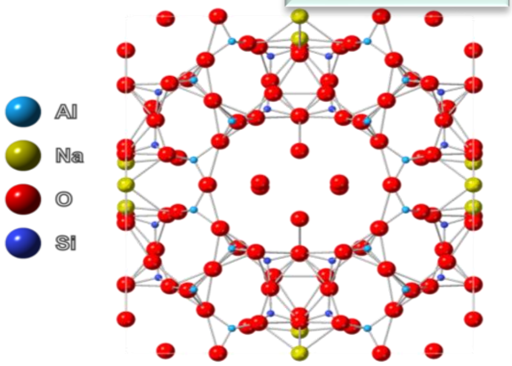


Why MOFs? The Evolution of Porous Materials

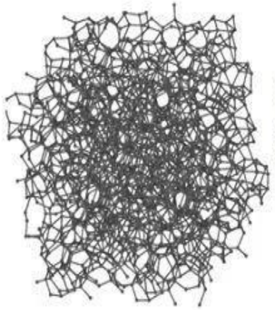
Property	Zeolite	Activated Carbon	MOF
Composition	Crystalline aluminosilicates (Si–Al–O framework)	Amorphous carbonaceous material	**Metal ions/clusters coordinated to organic linkers**
Structure type	Highly ordered, rigid framework	Disordered, porous network	**Highly ordered, tunable crystalline framework**
Pore size	Uniform, typically < 1 nm (microporous)	Broad distribution (micro–meso–macro)	**Adjustable from micro to mesoporous by linker design**
Surface area (m^2/g)	300–800	500–2000	**Up to >10,000**
Chemical tunability	Limited substitution (Si/Al ratio)	Possible surface oxidation or doping	**Highly tunable via linker and metal choice**
Thermal stability	Excellent (up to ~700 °C)	Good (up to ~500 °C)	**Moderate (usually <400 °C, depends on MOF type)**
Crystallinity	Crystalline	Amorphous	**Crystalline**
Hydrothermal stability	High	Moderate	**Variable (can be improved by metal/linker selection)**
Applications	Catalysis, ion exchange, gas drying	Adsorption, water/air purification, energy storage	**Gas storage, catalysis, drug delivery, sensing, separations**

Evolution → MOF

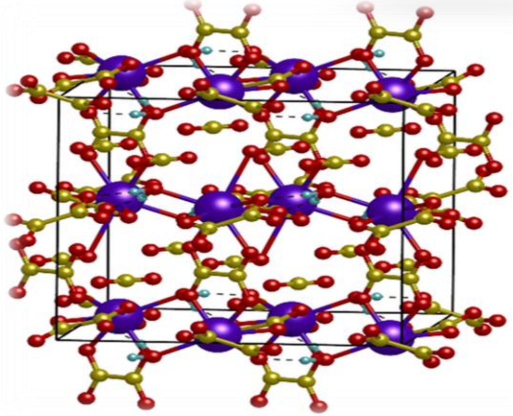
Zeolite



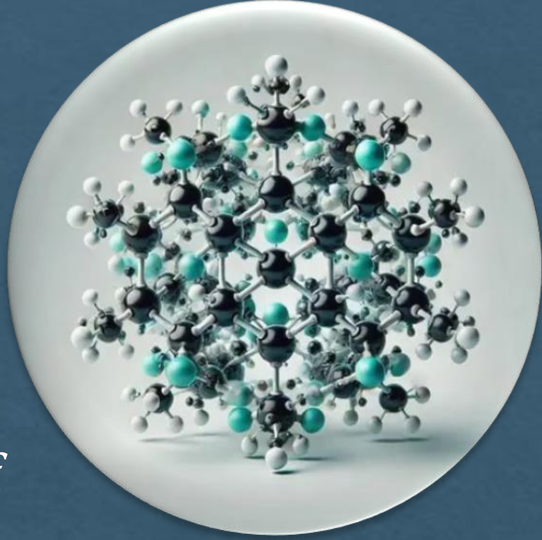
Activated Carbon



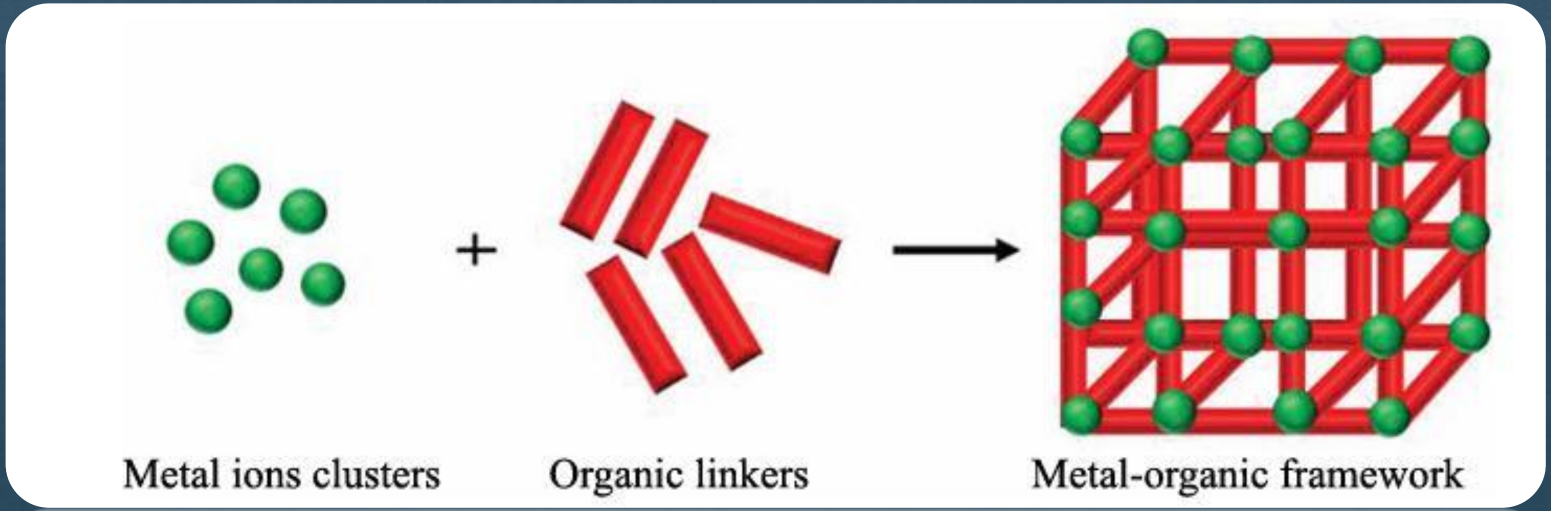
MOF



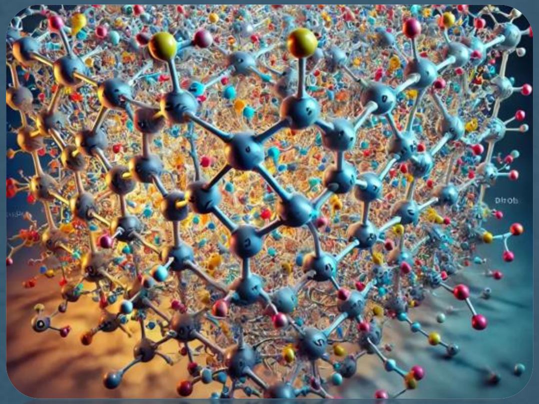
Metal-Organic Framework (MOF)



A Metal-Organic Framework (MOF) is a porous, crystalline material made of metal ions or clusters linked by organic ligands, forming tunable, highly porous structures with large surface areas.



Key Features of Metals and Organic Linkers in MOF Design



Metal Node: The metal serves as the core of the framework, playing a crucial role in determining the stability, structure, and overall functionality of the MOF.

Desirable characteristics of the metal:

* High coordination capacity (to form extended 3D networks)

* Ability to form stable bonds with oxygen or nitrogen donor atoms

* Suitable chemical and thermal stability

* Possibility of paramagnetic behavior or catalytic activity, depending on the intended application

Common metal ions used: Zn^{2+}, Cu^{2+}, Co^{2+}, Ni^{2+}, Fe^{3+}, Al^{3+}, Zr^{4+}, Mg^{2+}, Mn^{2+}, Gd^{3+}

Organic Linker: Organic linkers act as bridges connecting the metal nodes, defining the pore size, shape, and overall topology of the MOF.

Desirable characteristics of the linker:

•Presence of electron-donating functional groups (–COOH, $–NH_2$, –N=N–, –OH, imidazole, triazole)

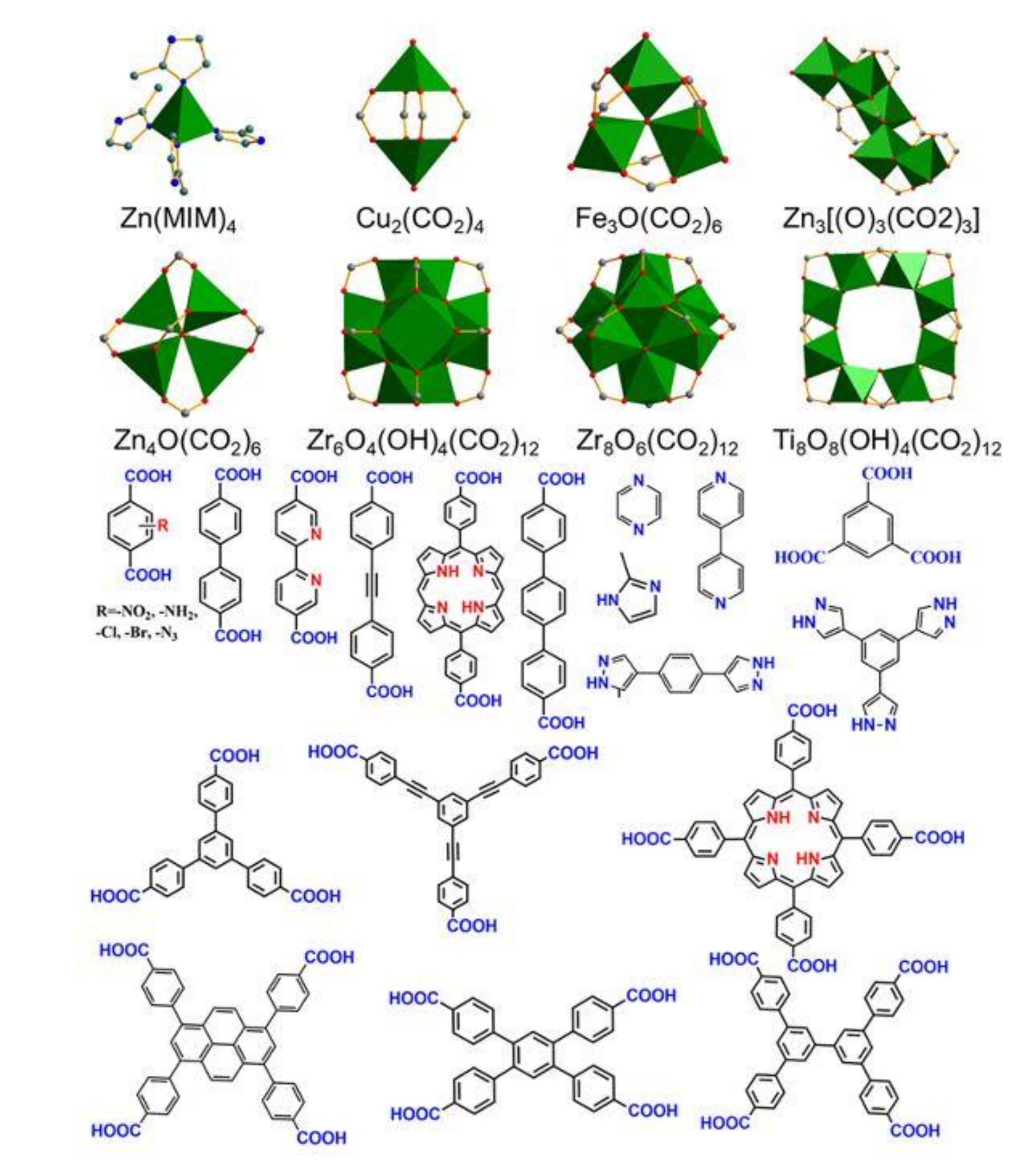
•Multidentate nature, capable of coordinating with multiple metal centers

•Stability under reaction conditions

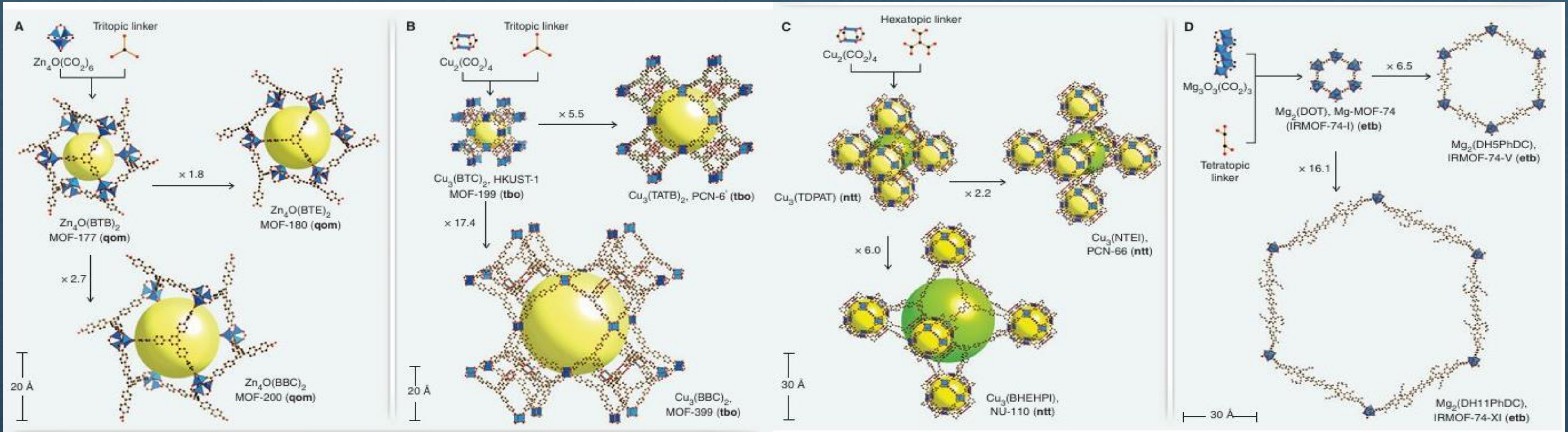
•Adjustable length and flexibility to tune pore dimensions

Common linkers: BDC (benzene-1,4-dicarboxylic acid), BTC (benzene-1,3,5-tricarboxylic acid), imidazole, triazole, bipyridine

Some representative SBUs and organic linkers for MOFs.

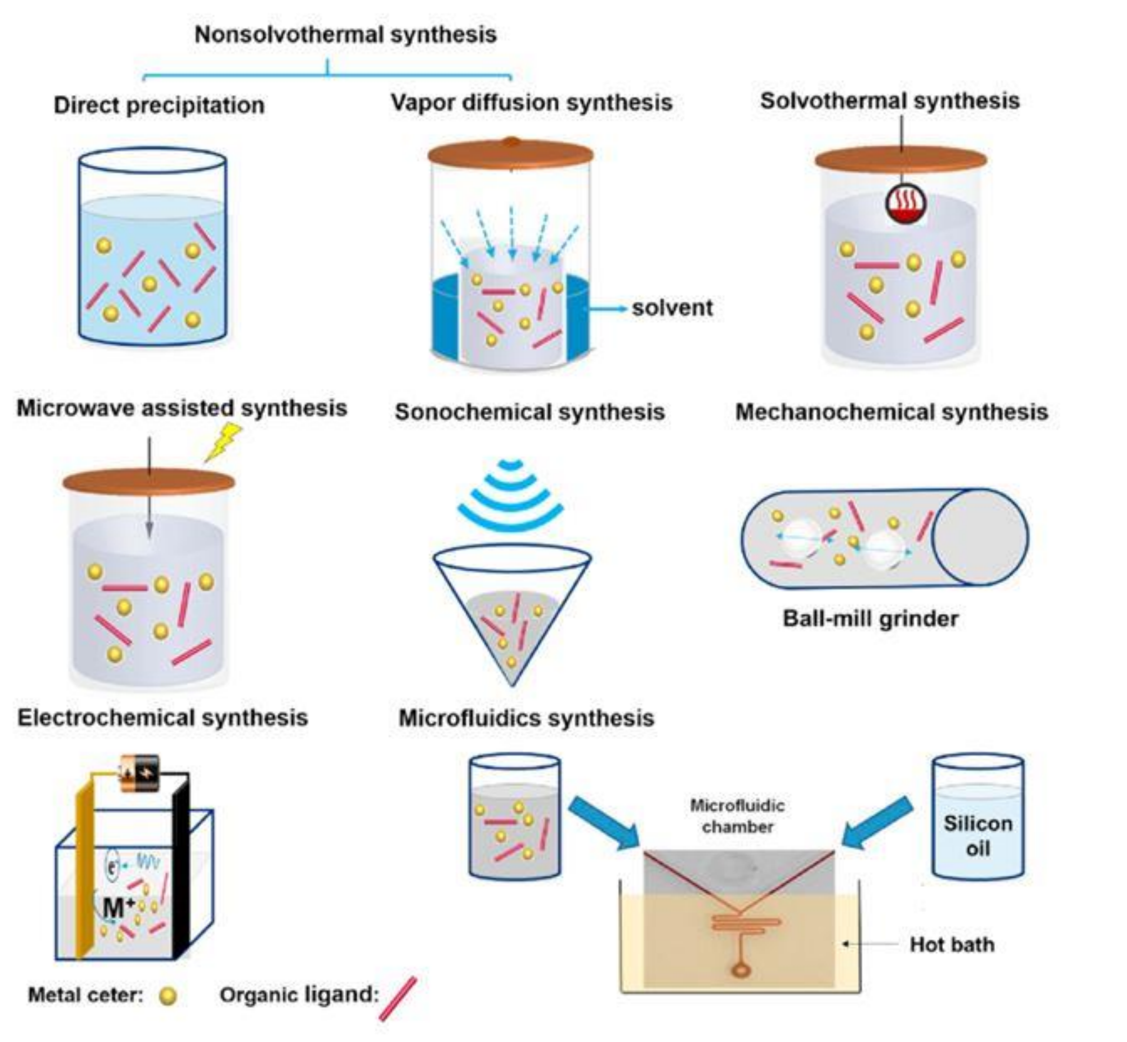


Effect of Metal and Ligand Type on the Structure and Porosity of Metal–Organic Frameworks (MOFs)

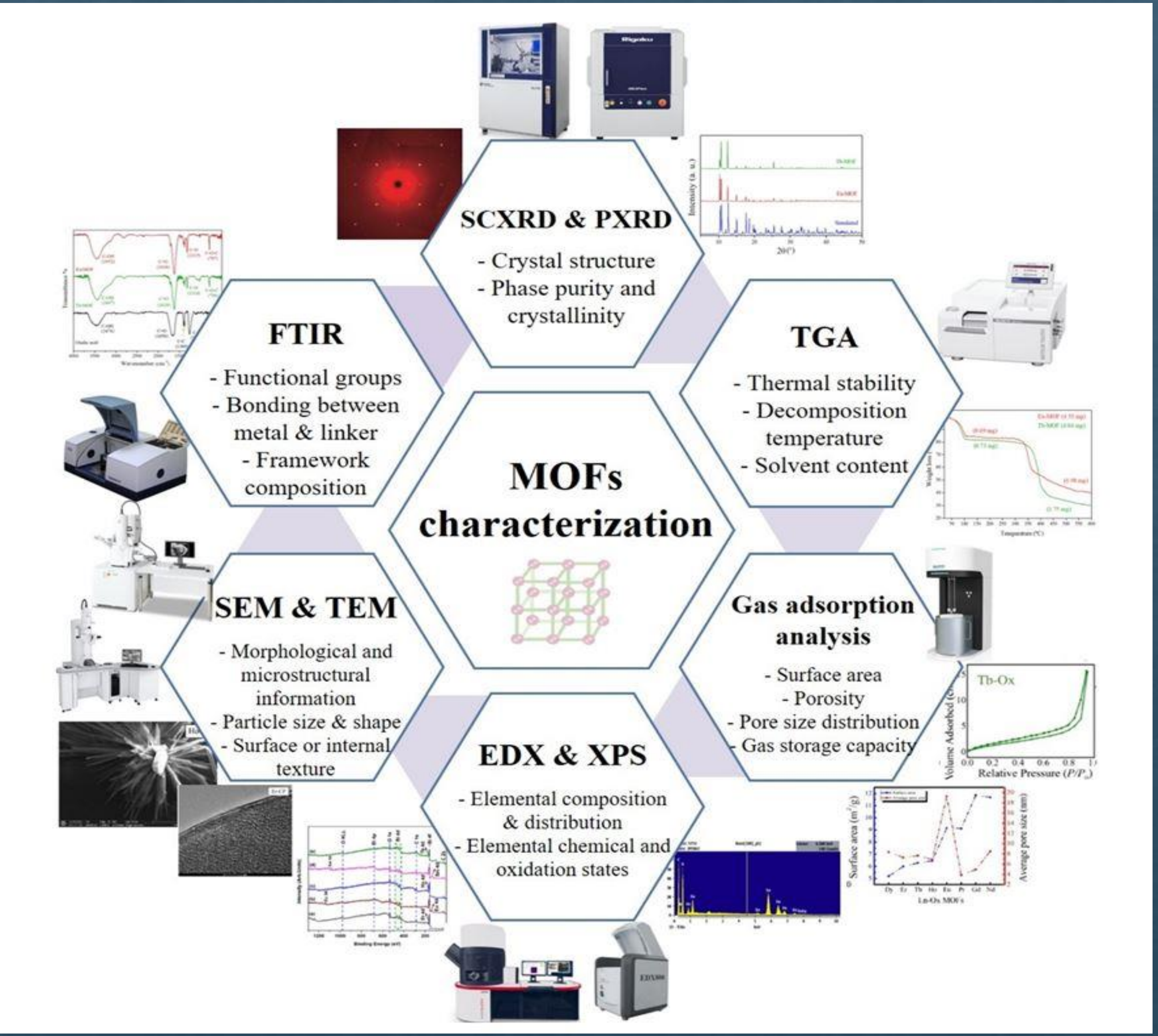


Thus, the rational design of ligands and the appropriate choice of metal centers are key to controlling the structure and functionality of MOFs.

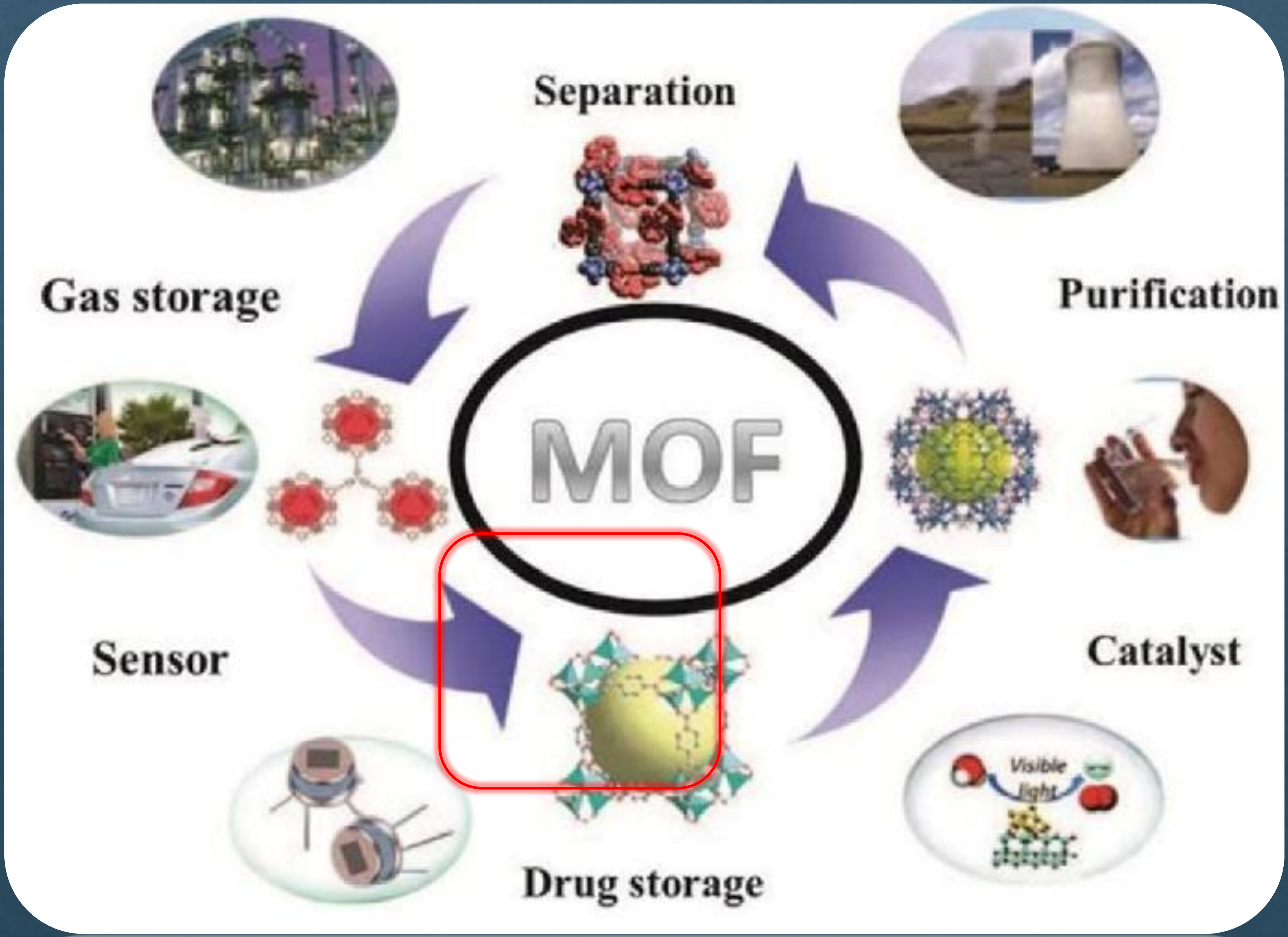
Overview of MOFs synthesis methods.



Overview of the basic characterization techniques for MOF materials.



Application of MOFs



Metal and Ligand Selection for Biomedical and Drug Delivery Applications

❖ Suitable Metal Centers

- Low toxicity (< 0.1 ppm free metal in blood)
- High coordination stability (log K > 10)
- Ion-exchange ability for drug or imaging probe release

Zn^{2+} (ZIF-8): Non-toxic, stable at pH 5–7, ideal for pH-responsive drug release (e.g., 5-FU).
Fe^{3+}/Fe^{2+} (MIL-100/101): Biodegradable, MRI (T_2 contrast), up to 30% drug loading.
Zr^{4+} (UiO-66): Extremely stable (pH 1–11), biocompatible
Mn^{2+} (Mn-MOF): Paramagnetic (MRI T_1 contrast), low toxicity when optimized.

❖ Suitable Organic Linkers

- ✓ Biocompatibility and metabolizable or excretable ligands
- ✓ Small size (MW < 300 Da) for porosity (2–5 nm)
- ✓ Strong M–N or M–O bonding for hydrolytic stability

Imidazoles (e.g., 2-methylimidazole): In ZIF-8; cheap, pH-responsive, stable.
Carboxylic acids (e.g., BDC): In MIL-53; high drug loading (20–30%), biocompatible.
Porphyrins / Tetrapyrroles (e.g., PCN-224): Fluorescent, useful for PDT and bio-imaging.

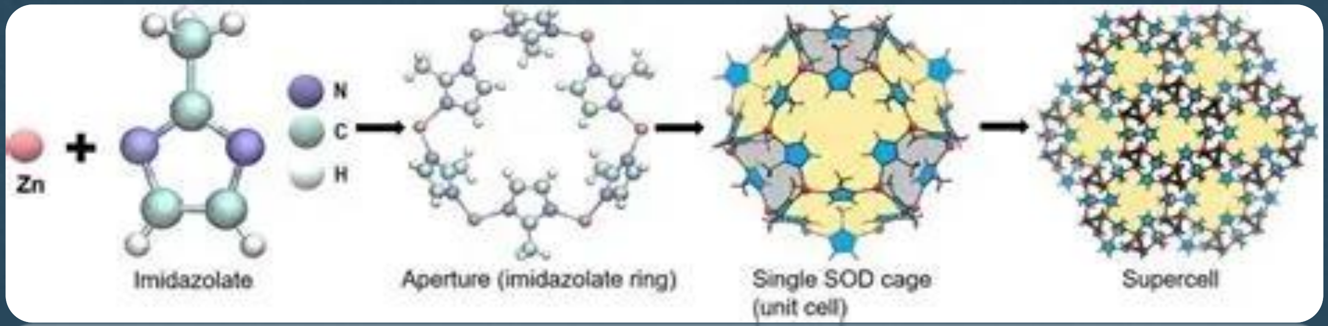
Desired Properties of MOFs for Biomedical and Drug Delivery Applications

Property	Optimal Range / Requirement	Purpose
Particle size	50–200 nm	Efficient cellular uptake, long blood circulation, avoids RES clearance
Surface area	1000–2000 m^2/g	High drug/contrast agent loading (up to 40 wt%)
Thermal & chemical stability	Stable up to 300–400 °C; pH 4–8	Resistance to physiological and acidic environments
Porosity & pore volume	Pores 2–5 nm; 0.5–1 cm^3/g	Loading of diverse drugs (e.g., doxorubicin, 5-FU)
Functionalization	PEG, silica, or antibody coating (e.g., folate)	Targeted delivery and reduced toxicity
Controlled release	pH-responsive (≈80% at pH 5 vs 20% at 7.4); stimuli-responsive (light, heat)	Sustained and site-specific release

Optimized particle size, high porosity, and smart surface functionalization make MOFs ideal nanocarriers for safe and targeted drug delivery.

Comprehensive List of Drugs Encapsulated in ZIF-8

Drug	Application	Loading Method	Loading Capacity (w/w)	Success Rate
Doxorubicin (DOX)	Breast, lung, blood cancers	One-pot / Impregnation	20-30%	80-85% release at pH 5-6, targeted toxicity on cancer cells
5-Fluorouracil (5-FU)	Colorectal, breast cancers	One-pot / Co-crystallization	~85% (release)	85% release in 12 hours, combined with C-dots for imaging
Curcumin (CUR)	Breast, cervical, liver cancers	Impregnation / One-pot	28-49%	3x release at pH 5, 76.8% toxicity on HeLa, reduced drug resistance
BIBR 1532	Telomerase inhibition (various cancers)	Encapsulation	-	Enhanced cellular uptake, G0/G1 arrest, low toxicity to healthy cells
Benznidazole (BNZ)	Chagas disease, potential anticancer	Impregnation	-	Improved bioactivity, slow and stable release
Homoharringtonine (HF)	Melanoma (skin cancer)	One-pot (PEG/ZIF-8@HF)	41.45%	Strong anti-tumor effect, increased caspase-3/8, reduced MMP-9
Paclitaxel (PTX)	Lung, breast cancers	Encapsulation (ICG)	-	80% tumor growth inhibition, pH/NIR-responsive release, imaging
Methotrexate (MTX)	Liver, prostate, stomach cancers	Impregnation (CS/ZIF-90)	-	pH-responsive release, high selective toxicity
Ibuprofen (IBU)	Initial test (anti-inflammatory)	Impregnation	-	pH-sensitive release, enhanced stability
Caffeine (CAF)	Delivery of small molecules	Impregnation	28%	Successful loading, controlled release
Bortezomib (BTZ)	Breast cancer	Encapsulation	-	Synergistic effect, controlled release
EGCG (Palmitate derivative)	Anticancer antioxidant	Impregnation	-	Enhanced stability, anti-tumor effect



Future Challenges of MOFs in Biomedical

1.Toxicity & Biocompatibility

Heavy metals (Gd, Cu) may cause toxicity in biomedical uses.

2.Industrial Scalability

Upscaling from lab (mg–g) to industrial scale (kg–ton) is costly and complex.

3.Stability in Biological Conditions

Degradation under variable pH or enzymes reduces efficiency.

4.Cost & Accessibility

Expensive linkers/metals (e.g., Zr, porphyrins) limit commercialization.

5.Targeted Tunability

Need precise control of porosity & functionalization for disease-specific delivery.

6.Regulatory & Clinical Approval

Clinical translation needs strict toxicity and metabolism assessments

References

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Thanks

for your attention