The Chemistry of Nature, Reimagined

Nature uses complex molecules to perform miraculous feats, such as turning sunlight into sugars. A new class of extremely porous crystals is making that kind of complexity accessible to humans.

SO MANY OF THE THINGS NATURE DOES effortlessly, such as using the Sun’s light to fuel growing plants, have been virtually impossible for chemists to emulate. But now, they have a tool that is helping them harness the same type of complex chemistry found in nature and design new kinds of structures virtually at will.

The secret is a type of nanoscale cage called a metal-organic framework and its purely organic counterpart, a covalent organic framework. They are like crystals built from Tinker Toys, with metal- or carbon-based hubs connected by rod-like molecules. What makes these crystals unlike any type of structure before is that they are mostly air, so they can trap molecules inside, where those molecules can react chemically with the cage or with others trapped nearby. These “shotgun marriages” may hold the key for producing liquid fuels from sunlight, or mopping up toxic chemicals in the environment, or learning more about the complex molecules essential to life.

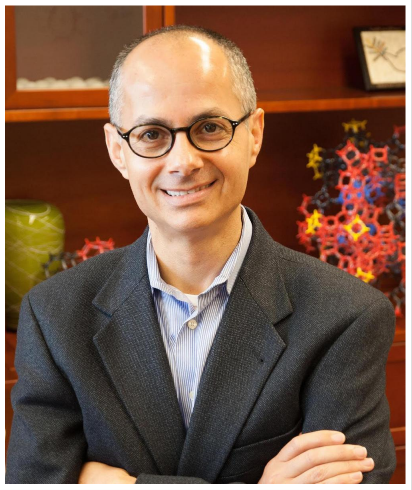
Recently, Omar Yaghi, co-director of the Kavli Energy NanoSciences Institute, showed how to use these open frameworks to study molecules that are hard to isolate any other way, and to make strong textile-like woven structures chemically. To discuss this new chemistry and how it could transform fields as diverse as transportation, fuel production, electronics and medicine, The Kavli Foundation brought together three research leaders for a roundtable discussion.

The participants were:

- **OMAR M. YAGHI** – s a professor of chemistry at University of California, Berkeley, and co-director of the Kavli Energy NanoSciences Institute and the California Research Alliance by BASF. He is considered the inventor of metal-organic frameworks and covalent organic frameworks. Between 2000 and 2010, he was the second most cited chemist in the world.
- **JOSEPH HUPP** – is a professor of chemistry at Northwestern University and a Senior Scientist in the Materials Science Division at Argonne National Laboratory. His research group studies the application of MOFs to artificial photosynthesis, chemical separations, molecular sieves and fuel storage.
- **THOMAS BEIN** – is the Chair of Physical Chemistry and a professor of nanoscience at Ludwig-Maximilians-Universität München in Germany. The Bein Research Group is investigating the use of MOFs and COFs in electronics, solar cells and targeted drug delivery.

The following is an edited transcript of their roundtable discussion. The participants have been provided the opportunity to amend or edit their remarks.

THE KAVLI FOUNDATION: ***Professor Yaghi, what's the advantage of this new way of doing chemistry using metal-organic frameworks (MOFs)?***



Omar Yaghi is the co-director of the Kavli Energy NanoSciences Institute and the California Research Alliance by BASF. (Credit: Berkeley Lab)

OMAR YAGHI: If you think about how humans typically do chemistry, it usually involves some combination of high temperatures and high pressures, and it produces a lot of waste products in addition to the chemicals we want. This limits us to making fairly simple and small molecules.

Now compare that to nature. Biological systems conduct their reactions at room temperatures and pressures, and make the same molecule repeatedly and with no waste. And they often make molecules so large and complex, we are still trying to understand their structures.

For a long time, chemists had no way to make complex chemical structures the way nature does, so they usually wound up with a mess. Now, with these metal-organic frameworks, we have an easier way to do this, because they are essentially scaffolds. Like the framework of a skyscraper, they have a very precise, open, repeating structure. We can bind groups of chemicals onto them.

This lets us create something similar to the complex environments found in nature. An example of this is enzymes—proteins that trigger chemical reactions in living things. They only work if their shape matches the molecule they are designed to react with, and if their active site, where the reaction takes place, has the right molecules surrounding it. Change those molecules or its shape and it does something completely different. With framework crystals, we can create an environment similar to an enzyme's, with a specific shape and a specific active site that initiates a reaction.

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This is what the future of chemistry is really about—breaking and forming bonds in a selective way. Our work makes this possible because we can design the scaffold and modify it so that it acts very selectively.

In fact, in some ways we can go beyond what nature does. For example, we can create these structures that are more stable than their natural counterparts.

TKF: ***So you don't have to duplicate nature to create the type of reactions nature does?***

YAGHI: Exactly, but we do have to learn from nature.

JOSEPH HUPP: I agree. There is a very important difference between biomimicry and bioinspiration. Living organisms do many things to stay alive, and they ask a lot from their biochemistry. These open frameworks aren't alive, so we can zero in on the pieces of that biochemistry that we need.

Also, as our fundamental knowledge about these frameworks increases, we have increased our ability to do more with them. For example, we have learned how to build structures with wide pores. This allows large molecules, such as proteins, the building blocks of life, to enter them.

And we still have room for other chemicals to enter and react with those proteins to make whatever it is we want.

Joseph Hupp is a professor of chemistry at Northwestern University and a Senior Scientist in the Materials Science Division at Argonne National Laboratory. (Credit: Northwestern University)

YAGHI: We can also change the chemistry along the length of the metal-organic framework so after a molecule undergoes one reaction, it can move through the framework and undergo a sequence of additional changes to produce a specific product.

HUPP: Yes, and remember, the molecule is moving through the framework very quickly, at a rate of one nanometer per nanosecond. In that environment, we could make unstable intermediate chemicals that last for only a single microsecond, and we would still have plenty of time to modify them. So, these open frameworks make possible a type of chemistry that only cells seem to know how to do easily today.

TKF: ***And we can build these open frameworks to achieve specific outcomes?***

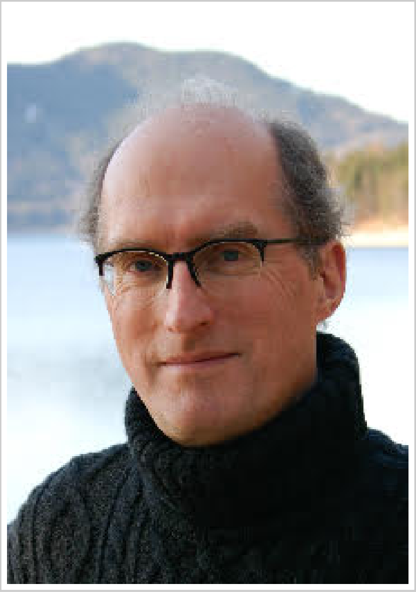
HUPP: And for different environments.

Our collective understanding of design principles has advanced greatly, and we can make open frameworks that are chemically pretty close to bulletproof. It's now possible to make metal-organic frameworks that split water into are chemically pretty close to bulletproof. It's now possible to make metal-organic frameworks that split water into oxygen and hydrogen, that work under water, and that stand up to extreme conditions. This enables us to do reactions faster or to do reactions that nature cannot manage. Thanks to everything we have learned by studying them over the years, a good chemist can make frameworks with just the right pore size, framework presentation, hierarchy of channels—whatever is desired—because we understand the rules of how to make them.

THOMAS BEIN: There are many interesting and very stable structures. We just need to learn how to tune these properties.

HUPP: That's certainly much of the fun of creating new chemistries. In many labs today, we are designing open frameworks to do exactly what we want them to do.

TKF: ***So what does this new chemistry allow us to do that was once difficult or impossible?***



Thomas Bein is the Chair of Physical Chemistry and a professor of nanoscience at Ludwig-Maximilians-Universität München in Germany.

HUPP: It revolutionizes the development of green energy. With this tool, we can more closely mimic photosynthesis, which is how nature converts sunlight into energy. The difference is that nature uses sunlight to turn water and carbon dioxide into sugar, and creates oxygen from water and carbon dioxide. We want to turn water and carbon dioxide into liquid fuels.

TKF: ***Mimicking photosynthesis has been one of rough patches for developing solar energy.***

HUPP: Yet nature does this every day by harnessing light from big chunks of the color spectrum using complex molecules. How do we duplicate its complex systems? One of the breakthroughs involves building frameworks layer by layer, like a sandwich. And you can tweak the chemistry of each of those layers so it captures a different slice of the color spectrum. So instead of trying to create one very complex molecule, we make a bunch of simpler molecules that work together to do the same thing.

TKF: ***How difficult is it to make these "sandwich" structures?***

HUPP: Building such a complex structure one layer at a time would outlast the patience of anyone. But it would not outlast the patience of a robot. In our lab, we have five robots building them.

BEIN: Layers are useful in other ways, too. Ordinarily, to make polymer solar cells that convert sunlight into energy, you need to build very precise, aligned structures to control how the polymers interact with one another. This is a very difficult, empirical process. But using molecular frameworks can give us exactly the right alignment for mimicking the behavior of an organic photocell. It's a much simpler process.

> *"These open frameworks make possible a type of chemistry that only cells seem to know how to do easily today."—Joseph Hupp*

TKF: ***Professor Yaghi, using covalent organic frameworks (COFs), you become the first person to weave together molecules like a fabric, something most chemists thought was impossible. Why is this significant?***

YAGHI: We make cloth fabrics by weaving threads in and out of one another. This creates a fabric that is very hard to pull apart. Chemists have spent decades looking for ways to manipulate molecules to do the same thing.

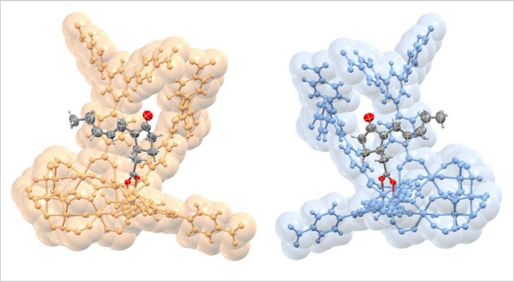
We can build framework crystals with part of this crossing structure. When they link together, they form molecules with the in-and-out structure of a textile. In fact, this structure is indistinguishable from a woven one. We may have made it in an unusual way, but it looks the same and the molecules lock together mechanically so it cannot ‘unzip.’ This means that one day we may be able to design tough molecular textiles that can carry out chemical reactions under conditions that might destroy conventional molecules.

BEIN: Omar's description of woven structures shows how far we have come. Not long ago, chemists were doing things like this by trial and error.

TKF: ***What are some of the other things we could do with these open frameworks?***

BEIN: We could use their pores to trap smaller molecules and study them. Nanoscale molecules get easily lost when we try to isolate them for study. But we could design framework structures to trap the molecules that interest us. Omar recently published an important work showing that this could be done with molecules ranging from a simple alcohol to a complex plant hormone.

Once we’ve captured them, we could use X-ray scattering or neutron scattering to take snapshots of their structure and how they interact with active sites in the framework. Imagine, we could see a chemical reaction as it happens. We could see how those molecules change shape and how they react when they encounter different active sites. We could examine the sequence of reaction steps, determine whether our theories are correct and use what we learn to create more effective chemical reactions.



Open frameworks can trap smaller molecules, enabling scientists to take snapshots of their structures without having to crystallize them. (Credit: Yaghi Laboratory)

TKF: ***In other words, use these open frameworks as laboratories.***

BEIN: Yes. And I also wanted to bring up something else we are working on—targeted drug delivery. Treating cancer might be an example. Through smart chemistry, we could place a medicine in the pores of an open cancer might be an example. Through smart chemistry, we could place a medicine in the pores of an open framework, then decorate the framework's scaffold with a combination of molecules that cancer cells recognize as food. The cancer cell will then hopefully and happily commit suicide by swallowing the framework and releasing the targeted medicine. We might be able to make them—or the smaller molecules they break down into—small enough to pass through the kidneys, which are the body's cleansing system. Or perhaps we could deliver them through the lungs or skin, or with an injection.

TKF: ***Is anyone putting this technology to work today?***

BEIN: Companies are now working on using these framework crystals to store natural gas and hydrogen for use as fuels in vehicles. The goal is smaller and safer fuel tanks, which will make these vehicles immensely more practical.

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YAGHi: In fact, the German chemical giant, BASF, has used metal-organic frameworks to store methane in vehicles fueled by natural gas. For the past three years, it has tested them on a fleet of automobiles in Germany and the United States. They have gone through more than 100,000 refueling cycles without loss of porosity or performance.

After 10 years of development, BASF has shown it can make tons of these materials and use them to create natural gas fuel tanks that will last the lifetime of a car. This is an affordable and practical technology, not a laboratory curiosity. Low oil prices make it difficult to market. But if oil prices start rising again, it will become more attractive for owners of natural gas fleets to deploy.

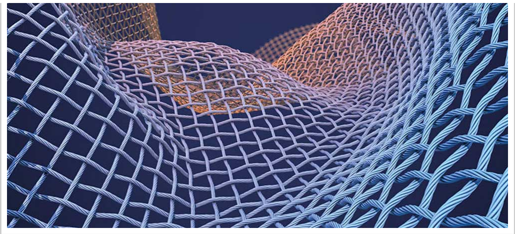
TKF: ***Should researchers be focusing on developing commercial products like that fuel tank or do we need a better understanding of the fundamental science first?***

HUPP: There are so many directions we could take this research, but let me put something provocative out there. Commercializing a real volume business, like methane storage, would truly start chemists thinking differently about framework materials.

Right now, nobody wants to be first. I think that Omar will get his trip to Stockholm—sorry to embarrass you, Omar—when metal-organic frameworks displace an incumbent technology because they have an economic advantage. Then the inhibitions will fall away and many, many applications will follow. But somebody has to break through first.

This is already starting to happen. NuMat Technologies, a spin-out from Northwestern, in partnership with Linde, a gas delivery from Northwestern, in partnership with Linde, a gas delivery company, now manufactures and sells a MOF-based system to deliver gases used to manufacture semiconductors under demanding conditions. I think we may see more companies like this in the future.

YAGHI: I think that BASF has demonstrated that you can make large quantities already. But for myself, I always emphasize the importance of basic science and study of properties. This is because taking materials from lab to market has little to do with science and a lot to do with markets, economics and other things we cannot necessarily control in the lab.



By linking open framework units, Yaghi's team has created a fabric of interwoven molecules, an accomplishment that has eluded researchers for more than a century. (Credit: Yaghi Laboratory)

Open framework crystals are going through a revolution in possible applications. A small group of researchers recently held a workshop and come up with 200 possible applications for them, as well as new properties that we and others are pursuing.

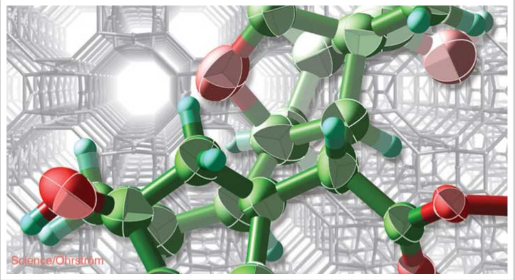
In this way, metal-organic frameworks are like other new technologies. There is a time to develop the basic science, a time to study properties and systems in detail, and then time to take those systems to market. So I think we're on track, and I know that we are changing the way chemists think about making materials. In fact, just recently several companies announced the release of a first wave of commercial MOF products into the market.

> *"I think we all feel overwhelmed with the beauty of the structures and the sheer excitement of the basic science. There are so many things to study, things that were not possible to do in the past. We once dreamed about sequences of reactions, building like nature, or creating organic circuitry. Today, these dreams are becoming part of the realm of the possible."—Omar Yaghi*

TKF: ***We've talked a lot about the potential of open framework crystals. Let's finish up with the challenges. What research gaps do we need to close?***

YAGHI: We should think about ways to create systems that, like biology, do more than one thing at a time. We should start thinking about how we might build a sequence of active sites, and how to characterize and control them. These are questions that will not only challenge chemists working with framework crystals, but the entire scientific field.

BEIN: My interests involve the electronic properties of framework



Open frameworks could be used to trap molecules so that they react with elements in the framework structure or one another. (Credit: Yaghi Laboratory) *structure or one another. (Credit: Yaghi Laboratory)*

structures. I would like better design rules to control the electrical interactions among building blocks in highly ordered structures. This is a case where even the smallest changes in the spacing and angles between atoms can have an impact on electrical behavior, and they are going to be important in the future.

HUPP: I feel like a fish swimming in water, because there is so much to do everywhere I look. When discussing thesis projects with my students, I always ask, "Is there any better way to do this?" If they think not, then they have found a worthy problem. As far as my own work, the water I'm swimming in involves seeing just how far we can go in making enzyme-like environments and catalysts, and using computer models to change how we do chemical reactions.

YAGHI: I think we all feel overwhelmed with the beauty of the structures and the sheer excitement of the basic science. There are so many things to study, things that were not possible to do in the past. We once dreamed about sequences of reactions, building like nature, or creating organic circuitry. Today, these dreams are becoming part of the realm of the possible.

—Alan Brown, Fall 2016

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