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Discussions of Session 3 — Reticular Chemistry and New Materials

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Omar Yaghi
I think we will just open the presentations for discussion. Questions from any of you about anything that you have in mind?

Kurt Wüthrich
Well, the word *complexity* has been very frequently used since yesterday. Should we not try to define what we really mean with complexity? Is it size? Is it lack of symmetry? Or is it too many panels on a single slide? Is it dynamics, where we add at least a fourth dimension to describing

structure, I mean time-dependent fluctuations. Is it a lack of periodicity? How do we define complexity? The word was used so many times in different connections since yesterday, that I think it would be very nice if we could come to some conclusion on what we want to say with complexity.

Omar Yaghi

Nature of course is the best teacher and, I think, *complexity*, for me, means the presence of a variety of interactions — weak interactions, hydrogen bonding, hydrophobic interactions, polar interactions — within an entity. But also, there is a landscape of energy, different energy levels that electrons can travel through. And also, there is a gradient, not just a gradient of composition, although that is a very important one, the gradient of composition, a gradient of interaction, a gradient of energy levels. And of course, there is also hierarchy in terms of structure, there is a hierarchical arrangement of molecules or compartments. All of those come together. And, of course, you want this to have a purpose. And, hopefully, directionality. I think all those things define *complexity*. My comment yesterday about supramolecular chemistry is that you can create complex systems very easily. But to control them, and to have directionality and purpose, is much harder. I think you saw today that we worked very hard, all of us, at making ordered systems. And now, because you can modify those ordered systems in different ways, covalently and non-covalently, now you can begin to build *complexity* without falling into chaos, which I called goo. This is the ideal area of growth, the marriage of supramolecular chemistry to what reticular chemistry was.

Makoto Fujita:

It is exactly the same question as I had yesterday. We should discuss what are *complex systems* or *complexity*. First, let us think of assembly. Weak interactions work between or among any molecules. But there are many, many miserable assemblies. Then we should not say this is the assembly. Only when the ordered structure is formed, then we can say that this is self-assembly or assembly. So, the order of the structure is necessary. And, in the same time and in a similar way, in complex systems, by networking there are many chemical events. Some order should generate, something ordered should be generated. In my opinion, the generation of constancy

or, in biology, *homeostaticity*: by the networking of many chemical events, the system will try to keep their constancy in the system. Maybe most people are interested in the life system. The most, the best complex system is life. And homeostaticity could be a target of the complex system. So, we should aim at self-constancy systems.

Joachim Sauer:

First of all, complexity is not disorder. And if we talk about complexity, there are different dimensions. Lots have already been said about complexity of structures. There are different organizations at different levels, and there may be a hierarchy. There is also complexity in the dynamic behavior, if different parts of the system have different time scales, are doing things at different time scales. And there is complexity in the reactivity: you may have a system where you may have just one or two important steps, but then you may have, in heterogeneous catalysis, reaction systems where you have possibly 130 steps to take into account, including heat and mass transport. So, there are different dimensions. And when it comes to, you have asked this question, *symmetry*, also the absence of symmetry is not complexity. It would be that you have in a structure, at different levels, different symmetries that you make. You have building units that have some symmetry, and then you have an organization, which may have a different symmetry or no symmetry.

Arne Thomas:

After all these very elaborated answers from my colleagues, we probably also have to confess and be honest that *complexity* is often just another term for "we don't understand". When I read "there is a complex reaction mechanism", "there is a complex structure" or something, very often this just means "I don't understand this structure" or "I don't understand this complex mechanism". This is just something we have to be careful with. Always this "complexity" sounds better than "I don't get it". I do think to understand complexity, one has first to reduce complexity. This is why we all try to make more defined materials to have a chance to understand these materials better. And it would be for me a less complex material, though it might be a multifunctional material, but as long as I can understand what happens in this material, I say then this is not complex anymore for me.

Xiaodong Zou:
Regarding complexity, I agree with Arne Thomas that you do not understand, but we should actually make use of these opportunities. We usually think about simplified things, like you want to look at one material, pure phases, and simple structures, but the systems are complex, in the form of, like, when you talk about the functionality. It can be used in different ways of generating materials in the complex system, or in trying to understand this complex system, and in being able to have characterization tools, to be able to develop, to study, this complex system. So that changes the *complexity*, until something we really understand maybe becomes simple.

Chad Mirkin:
I do not have a lot to add. I think it is a term. First of all, I did not use it, I want to say that, and I do not think you heard me use it. But second, I think it is very similar to the whole evolution of the term *self-assembly*, which meant many things to many people. The substance of it, is that complex multicomponent systems often have properties that go beyond subunit-based systems. And that is an important pursuit, understanding primary structure, secondary structure, tertiary structure, and then function that correlates with that structural understanding, that structural control. To me, that is the ultimate goal in all this: how do you begin to zip together subunits to create structures that are "complex", but more importantly, have properties that you cannot realize from the subunits themselves. I think there are many examples that we heard today and yesterday, frankly, and there will be many more from that type of pursuit.

Kurt Wüthrich:
I would like to follow up with a specific question to Professor Fujita. You showed to us that with a single parameter, you could go to higher order structures of a given type. Now does this mean that you get more complexity, or, because you now handle this with a single parameter, it is actually a simple system?

Makoto Fujita:
In my understanding, the complex system is on the next hierarchy of the ordering. Weak interaction of molecules can induce their self-assembly events. In a similar way, weak interaction of chemical events, so chemical

reactions, can induce their self-ordering of the system. It is not there are events among the molecules. So, I do not like to use the term complexity or complex system for making a structure from molecules only. It is not the assembly of molecules, but the assembly of chemical events.

Omar Yaghi:
I think *complexity* is not necessarily or should not be confused with *complicated*. That is why my description originally is a structural based description. I do like the idea that complexity produces a function that is much larger than the sum of the parts, and I think that is important. So to me, glass is not complex. There is no recognition, there are no weak interactions, things like that, that you can talk about in terms of function and things like this, but hemoglobin is complex.

Ben Feringa:
Another aspect of *complexity*: you guys make all these fantastic well-organized structures. When I talk with my colleagues in solid state physics about properties, it is always about step edges, defects sites, all these things, which determine the properties ultimately to a large extent. Could you comment on that? Because that adds another dimension of complexity to the system: to go to real functions.

Omar Yaghi:
I think every system is complex at some level. I mean a lot of the structures that you saw, if you look in detail, these are average crystal structures, and there would be defects. If you look at them in a TEM, you can see sometimes missing linkers, you can see rings that are supposed to be hexane and some of them have five membered rings, some of them have seven member rings distributed here and there. So to me, if you look at all these systems in great detail, and move away from the average structure, they are very complex systems. Which reminds me to also say that complex systems also have perturbations along the landscape of the composition.

Arne Thomas:
I think also important is, of course, to talk about the difference with solid-state chemistry structures, where, as you said, point defects, step defects,

and so on, have a huge influence on the bulk properties of such materials. Most of the materials we were talking about are actually molecular entities, which are connected by strong bonds. It is actually then the molecules that count, and not so much the bulk property. If you think about hydrogen storage or CO_2 separation, or what I have shown, there is actually a catalyst sitting there. If there is a defect, I have the feeling, it is not making such a big effect like in the solid state structure, where you look at the bulk property band structure, and so on and so forth. We see that, when we really get out of crystallinity, that then the properties of such materials change. So, we should not go away too much from the ordered structure, then something changes, but as we are actually talking most of the time about the function of the molecular entities in these materials, it is ok, I think, and there are some termination defects or something.

Ben Feringa:
I am happy to hear that. Because all the time with these band gaps, the energy levels for conductivity but also for catalysis and so on, and also we know from zeolites: that plays a crucial role. So, engineering these kinds of sites might be another challenge for the field.

Chad Mirkin:
But it is more complex than that and more difficult than that. Take the synthesis of the particles that I talked about. We can beat our chest and we can make 225 million distinct particles on a surface, which is true, in a four by four centimeter area. But when you get down to the individual particles, no two particles are exactly the same, the orientation of the particles, or even the composition differs. So the way we get to that is actually to use numbers, to use redundancy, to use the ability to make many things that are effectively the same, and look at all of them in one shot. Let us not miss one because of some of aberrations you are talking about, and then focusing on the actual structures that are giving us the activity that we see. But it is a difficult problem, because these systems are multiparameter, and their complexity makes them interesting, but also makes it very difficult to really pin them down.

James Liao:

If we try to define complexity, perhaps we can borrow the definition from mathematicians, where complexity is a property of a non-linear system. If you have a linear system, then typically you can predict everything, from the beginning to the end. It is completely predictable. If you have a non-linear behavior, nonlinear structure, sometimes you get to this bifurcation behavior, and all kinds of these strange attractors, strange behavior, emerge. So that is one line of origin, from where the word complexity came from. But now we use that word in the chemistry context, where things are more static, that is not that dynamic, but I am sure we can find something that is analogous to the dynamic complexity that mathematicians use.

Joachim Sauer:

Coming back to Ben Feringa's question about the role of defects and steps. We have already discussed, and I have mentioned it in my presentation, that you may have imperfections, and they may play a big role. I have briefly shown largely varying isotherms measured for the same nominal material, which change loading per metal site between two and four molecules per site. And if you look in details, this has to do with the synthesis process, so the role of steps and these things. So when it comes to electronic properties, then of course we would have the same problems as they have. If we have transition metal ions, the electronic structure maybe different if we have defects in the system. And if we go to diffusion, for example, then the question appears what happens at the surface of the crystallite. From zeolites, we know very well that there is this discussion of a possible barrier and the effect on the intracrystalline diffusion, in-out diffusion, and then the transport in the mesopores of the particles, which is finally in the interest of the user of these materials.

Xiaodong Zou:

In terms of defects, I would say that all these deviations from the periodicity of structures — for example like multivariant structures where you do a functionalization so that you have different functions, and also the

metals can be changed — generate multiple components in your structure. I think this actually will be a very positive way of making new functions into the material. Of course, the characterization will be challenging, and it needs to be developed.

Ben Feringa:
I had no intention to make a negative comment, I just wanted to say that defects and all these kinds of things are intriguing and offer all kinds of opportunities, and Nature probably knows how to handle it. I again refer to a cell. There are many things that a cell knows how to control, and in catalysis, for instance, this plays a key role. It offers also a lot of opportunities for us, to introduce function and so on.

Donald Hilvert:
You have shown all these beautiful structures, and it looks like the chemical instruction to create them is fairly well understood. How reliable is your ability to impart specific functions on these structures, and is it always mediated by adding specific metal ions, are these new coordination sites, or additional functionalities?

Omar Yaghi:
I can give you the example of water, because we ultimately figured out exactly the absorptive sites of each water molecule in a structure, exactly how the water is sitting, exactly the hydrogen donor and hydrogen acceptor in the structure, and exactly the geometry of how it is sitting. Now you can design, incorporate linkers that will enhance or strengthen the interaction or weaken the interaction, depending on what you really want, and at what humidity you want to take up the water. So there is a lot of design going on there. I think in terms of designing the MOF itself, because of the multi-metallic nature of the sum of the building units in MOFs, there is always uncertainty whether you are going to get a six-connected multimetallic unit or a four-connected one. But once you make one member of a family, you can develop the rest of it, change the matrix functionality and everything like that. You can know a lot about the system. With COFs, that is completely different, because the COFs, like what Arne Thomas was talking about, their building units do not change during the reaction.

Only the linkage between them is what forms, and so they remain the same. So, in fact, they are made by design, because the building units remain intact during the reaction. So, there is a lot of design in COFs, there is a lot of design once you understand the system in MOFs, and especially if you are lucky to get the absorptive sites of gases, then there is a tremendous amount. That is why in my talk yesterday, I said we chemists are surgeons, because you could instead of a pyrazole dicarboxylate linker for a harvesting MOF, you could introduce an oxygen in a five-membered ring, a furan dicarboxylate, in a structure exactly the same as the one with the pyrazole, thereby weakening the interaction between water and the framework. And you could also mix those two together and modulate the hydrophobicity, so you can do a lot.

Chad Mirkin:

It is a really interesting question, because I did not make it clear. A distinction between how molecular architectures are engineered and how colloidal crystals with DNA are engineered, is that while we talk about the particle building blocks' atom equivalence, there is a fundamental difference, and that is that the bonding is independent of atom identity, and that is just not true in conventional chemistry. That actually dramatically simplifies the design space, because it now distils down to geometric arguments, and how things fit together to maximize duplex formation or hybridization. And what that allows you to do now, is engineer structures that we do not even see in Nature. I mean, we have now six that have no mineral equivalent. It allows you to dial in bond length, based upon the length of oligonucleotide. It allows you to dial in crystal habit, which you cannot do with conventional systems. And the reason that is so important is — connecting with what you said, that it feels we have now the design space down — that it is down. It is getting to the point where there will be computational programs that if you want to build a particular structure out of particles, the program will spit out the particle building blocks, the oligonucleotide sequences, required to get there. And then you can flip it around and do exactly what you were talking about, which is go to the physical scientists and say: "What property would you like? What structure should exhibit that property theoretically?", and I will make it based upon these design rules. And that is what I think is so exciting and what

I tried to share in the last slide, that we are getting to the point where we can design these types of materials properties not found in Nature, and properties that you design ahead of time and do not discover by happenstance.

Nicolas Giuseppone:
Related to the question of Ben Feringa and defects in your materials, but not related to the functions, just to the way you form your materials: Professor Yaghi, you mentioned that you use for your reticular approach less kinetically labile interactions than in supramolecular chemistry. So I am wondering how much relies on the correction of defects when you form your self-assemblies, or relies on the directional kinetic progression, crystallization of your material? And I would have the same question for the discrete MOF of Professor Fujita: how labile are they? Because you have shown this magic ring catenation, and I am wondering, looking at that, if in your MOFs, for instance Professor Yaghi, you can have reconfigurable structures. Can we for instance imagine catenation of 3D MOFs and materials brought from this approach?

Omar Yaghi:
Catenation of framework is a very interesting example, because when you make a MOF, let us say based on a primitive cubic structure, it naturally will want to interpenetrate. If the pores are large enough then it will self-interpenetrate. We think that this is happening at the very initial nucleation of the framework. Remember, what you are doing in the crystallization is you are trying to balance two things: you are trying to balance the self-correction with the kinetics of the reaction, to get you to form a crystal that you could see or you could analyze. So, along the way, depending on your reaction conditions, you could make a defective structure. And sometimes, we happen to look at it in TEM, sometimes we will see those defects in some of the granules that we are looking at. There are systems that no matter how large the pore gets, they will not interpenetrate. Mathematically it is just not possible because the synthesis codes for a certain connectivity, certain coordination, and in order to have that interpenetration you need a different coordination, and therefore it does not

happen. So I would say that a lot of the defects have to do with how you make the material. Sometimes, in some cases, some people have been able to introduce defects in a systematic way in a crystal, where they yank out one of the linkers at periodic intervals and then insert another linker with a different functionality at those sites, and this is proven through single crystal to single crystal to single crystal transformation. So it is done on the same crystal.

Makoto Fujita:
Even in the solid state, we sometimes observe the "magic rings" type behavior, I mean there is a kind of phase transition from the interpenetrated framework to the non-interpenetrated framework in the single crystal fashion. There are several examples. That means in microscopic views, even in the crystalline state, it behaves like in solution, it behaves like a liquid. So, although it is a crystal at macroscopic levels, it can still behave like a solution. So interpenetrated frameworks can be transformed into the non-interpenetrated framework.

Peter Palese:
We have heard about these wonderful structures in molecular entities. Are any of those new compounds toxic in humans or to humans? Do they cause cancer? Is there any concern for people working with them? Is that something which has come up?

Chad Mirkin:
I can give you an answer you probably will not expect, but the building blocks themselves, in the case of our particles we called them programmable atom equivalents, the other term for them is a spherical nucleic acid, they are actually used as drugs, and they are in six clinical trials, and in certain cases to cure different forms of cancer by gene regulation type pathways. That is probably not what you expected, but the interesting thing is that they have the property that they will go through your skin, so there is a concern working with them. We have to utilize a lot of protocols to make sure that we minimize contact, but we use that to actually create pathways to drugs.

Omar Yaghi:
There is an article in the Wall Street Journal today about Wenbin Lin's work at the University of Chicago on using MOFs for cancer therapeutics.

Karla Kirkegaard:
I was very intrigued by the topological consequences of some of your synthesis, and I was thinking about topology from biology. Sometimes, I guess, the interpenetration involved free ends, but sometimes you can get changes in topology that have to do with the reversibility of the bonds that you make. You break and rejoin them on the other side of what you pass through. I was wondering if you think the topological changes that surprise us have to do mainly with interpenetration, or sometimes it is the reversibility of the bonds that you make?

Makoto Fujita:
Nature uses many strategies for making interlocking structures. Sometimes it is very similar to ours: small fragments are preorganized, then enzymes will link the precursors to make highly complicated structures. And sometimes, just a single protein strand can fold and spontaneously knot. And previously, the number of knotted proteins was not so large, but in recent years, many, many knotted proteins were found. So, Nature has many strategies to make knots.

Karla Kirkegaard:
But in your case, you think it is a condensation of small pieces?

Makoto Fujita:
In our case, yes.

Omar Yaghi:
It would be interesting in his systems, because they are very dynamic, to take two entities that he made of different sizes, and try to not link them, but more, like join or melt them together, fuse them together, into some regularly shaped thing, and then in a reversible way. I do not know, have you tried that?

Makoto Fujita:
No.

Clare Grey:
It is really a sort of challenge to the panel and particularly to Chad Mirkin and others. A lot of these processes are very close to room temperature, and as an inorganic chemist you are really often restricted to binary oxides. I think the organic PVs in the lead-based halide perovskites are a beautiful example of where they can be processed to room temperature, and you control things. But I just wonder what the panel thinks about now trying to go up in temperature and explore a much wider range of materials and properties with the same sorts of unique, and very careful and precise approach? I know in metal-organic frameworks you use hydrothermal processes, but still you are restricted in the classes of materials you can do, for example, by doing these room temperature methods. I just wonder where the next directions are in terms of expanding the types of materials by putting temperature, and controlling of kinetics of reactions, to then get different classes in materials?

Chad Mirkin:
I may have left something out that was key. In the making of the particles in the chip, that is done at 500 to a thousand degrees. So those are high temperature materials. We can make high entropy alloys and lots of structures. You have seen quenching protocols, they can be employed. So those are materials that in fact are very compatible with high temperature. We can also make low temperature materials, like the perovskites, that is crystallization type of processes as opposed to a thermal degradation process. In the DNA based structures, those are inherently materials that are stable between room temperature and 220°C, depending upon the solvents you use and how you make them. But once made, they can and have been moved into solid state supports, silica for example, so that you can control architecture at low temperature and then move to supports that allow you to work at high temperature, to create all sorts of interesting catalytic architecture, for example.

Omar Yaghi:
I think in terms of the MOFs and COFs, there is a range of temperature from room temperature all the way to 300–400°C for the triazine frameworks. You want to stay cool enough, so that you do not burn off the C-H's that you need to introduce functionality down the road, right? Otherwise, we will finish off with graphite, which is not functionalizable or not as easily functionalizable. So I think you have to keep that in mind. There is a lot that you can do within 400°C.

Arne Thomas:
I agree, of course, that when you are working with organic materials or metal organic materials, you are restricted in temperature at some point. Already when you go to 500°C to make a synthesis, you see a lot of carbonization going on and then you are back to a carbon, which is a complicated material. I think, actually, the challenge we have is not so much going high with the temperature, but finding other covalent bonds where we can induce reversibility. The first COFs, were boroxine COFs from Omar Yaghi. If you put water on them, they dissolve again. Then came the imine networks, which are much more stable. And now we made vinyl-bonded bonded COFs, I do not want to go into detail, but these are C-C bonded, entirely C-C bonded COFs. No one thought ten years ago that it could ever be possible to make such a bond in a reversible fashion. And there are much more out there. This will be the way to go, I think. Temperature does not help so much there, but other tricks, so to say, to induce the reversibility. So far there has not been made any COF which is, for example, by transition metal coupled C-C coupling reactions. This is so far not possible. Any chemical reaction, any covalent bond is reversible of course, in principle. When you do Le Chatelier and actually get out, for example, some bromide as a potassium salt, then you shift the equilibrium so much to one side that you actually restrict reversibility. And this is something we all think about, I guess, because new linkages are always something which is interesting for us, as we add another point of functionality to a network.

Xiaodong Zou:
We have made use of temperature, also concentration, to modify MOFs because of the bond reversibility, so that you can extend, exchange the

linkers with different functionalities for the post synthesis processes. And also to expand the pores to larger ones, to change linker with a longer linker. And also to change topology, making use of this reversible self-assembled bonding. So in this, temperature is a parameter to play on.

Omar Yaghi:
I just want to say that if you want something higher than 400°C then you just work with carbonitride, but you will not get the functionalization that you would want, because now you are in the inorganic regime.

Gerald Joyce:
I have a question about informational complexity. You were talking about multivariate MOFs and differential occupancy within the lattice, and you raise this really intriguing possibility that there could be a linear ordering with regard to what the occupancy is. And of course, that information only has value if it could be propagated, if it could be read to an output channel. So, the question is: are there nearest neighbor effects, or what is the potential for nearest neighbor effects if you have a linear ordering? If it is periodic, that is boring. If it is a spin glass, that is boring. But if it is aperiodic and can be propagated, read out through nearest neighbor effects, then that is informationally interesting. So, what are the prospects for informational complexity of those systems?

Omar Yaghi:
What I love about those systems is that you are taking a very repetitive crystal and you are superimposing unique sequences of functionalities, of organic functionalities, or even you could do it with the metals, along the entire crystal. So now, if you are a substrate moving along the crystal, you are experiencing different microenvironments all the way from the beginning to the end. And we do not know anything about what is that sequence, but we know what the functionalities are, we know where they are, we know their ratio, we can vary all those components, so it is not a completely unknown system. So I think this is a computational problem. Let us say that I have a property, a catalytic reaction, that is sensitive to input and output. You can put in 10000 things and then look at how the product varies, and then work backwards to get to what potentially that sequence might be. I have no doubt that you can come up with that. We do not have

enzymes, like biologists, that can sequence that for us, but this is our poor way of doing it. The problem is that we, as chemists, are very uncomfortable with this. We like to make things, then characterize them, study their properties, and then push them to application. And what I am proposing, is that we skip the characterization and just use the system like a black box in terms of the sequence, and then let the computation and the machine learning give us some guesses as to what is going on. But we do see aggregation, as I mentioned, with NMR, you can do Rotational-Echo DOuble-Resonance (REDOR) NMR on these. It does not give you information on the molecular level, but in terms of the nano regime, you do see aggregation of one functionality relative to another. And in terms of the functionalities interacting, if they are fat enough, they do interact, and that does influence where they sit in the sequence.

Bert Weckhuysen:

We talk about thermal stability, but I think there is also something else important in, for example, catalysis. Are you stable in a solvent, water? What when there is, like in electrocatalysis, electrons and charging, pH? All these things when we would move to photo-, photoelectro-, or electrocatalysis, what would then happen with material? In zeolite or other heterogenous catalysis, what we sometimes have, is that the inorganic structure, even as perfect it is, will become partially in solution. Something is happening at the interface between the solution and the catalytic surface, and then after reaction it precipitates again. So we sometimes make the analogy, it was already made between other materials, zeolite is one example of it. What about metal organic frameworks, COF materials, etc, and do you see similar things?

Arne Thomas:

Probably, one general comment on stability, and actually Omar Yaghi can tell much more about this, I think, he has experience of 20 years. The people come and say: “But your MOFs are not stable, right, and your COFs are not stable”. I think there is misunderstanding in this because the inorganic chemists were the first ones who were actually interested in MOFs, of course, because there is crystallography and something in there, and they compared materials all the time to mesoporous silicas, silica

alumina, and so on. When we think about stability, we have of course, and there you are totally right, to think of what kind of conditions we have. I can just give you an example. I have one material which is made, you just look at it with wet eyes and it will flow away because it is absolutely not stable under humidity. But it is an anionic framework, and you can put it into an application where water is not present, like in a lithium ion battery, for example, in a membrane. And there, it is super stable and can do lithium channeling through this membrane. That is just one example. Of course, you think about catalysis, I fully understand, and there we will not do steam reforming with MOFs, I guess, and also not with COFs. If there is high temperature and water involved under these conditions, they are just not made for this. In electrocatalysis and photocatalysis, there is always the issue of photooxidation, for example, bleaching, which is happening. For example, these acridine dyes are known to photo-bleach with some time. We are not really good in making long-term tests: our long-term tests always mean 20 hours, and then we analyze the materials, and if it looks like before, everything is good. So therefore, I cannot give you a definite answer, but I think there are enough materials reported, for example Omar Yaghi talked about the new material for CO_2 separation, which is made in kilogram, ton scales, now in industry. They tested certainly for a long time.

Bert Weckhuysen:

I want to bring this to the positive side because, sometimes, what you have in heterogeneous catalysis is that you bring something in solution, and it is actually having an additional effect on the reaction mechanism. So, you could have like a heterogeneous-mediated catalysis, but it is still something at the near-surface that is happening. I think maybe these materials could also bring that to life, that is actually a positive thing of leaching.

Omar Yaghi:

I think the stability is a positive thing. It is just that Arne Thomas did not mention that, when you have olefin backbone COFs, they are stable in strong acid, strong base. It is not a secret, it is published. And even in corrosive environments, like n-butyllithium. It is a carbon-carbon bonded network, so the question of stability is an old question, it is no longer

there. We got MOFs that are cycling a hundred thousand cycles of water uptake and release in the middle of the desert, with absolutely no impact on the MOF. When you look deeply into what is happening in that MOF, there are water molecules that are seeds, and they stay in the MOF, and in a way they protect the MOF. We do not take them out, they just stay in there. They only represent less than 5% of the uptake. In terms of COFs, the stability issues are not there at all. You can cook them up in strong acid, strong base, nothing happens to these olefin COFs that we reported two years ago.

Arne Thomas:
Still, there are some materials where it could happen. Yesterday there was a question, I am not sure who asked, which sounded a bit like: what is better, homogeneous or heterogeneous catalysis? I have the feeling this is the answer what we have here, because we have molecular catalysis and an open framework structure. Some of them, for example, are anionic solids with immobilized cationic molecular catalysts. And then you cannot actually differentiate between homogeneous and heterogeneous catalysis, because the catalyst might work in solution, but if you filter the solid material, also the catalyst is separated. This might be exactly the effect you are referring to, and it happens in some of these materials too.

Omar Yaghi:
I think you also have to think about the applications, because you do not want everything to be a rock. You have to think about what kind of application you need, because in some cases you want the MOF to break apart. In fact, with the pesticide application, you want to encapsulate the pesticide in a MOF that, when exposed to the atmosphere, slowly releases the pesticide. So, it just depends on what kind of application you have.

Henry Snaith:
It is a very fascinating concept for the billions of material-manufacturing discovery processes. Two questions related to that. One is sort of a practical question: how do you get the different materials and compositions on the tips, before you put them into whatever vessel or whatever substrate you are synthesizing them on, or growing them on? How do you mix the

compositions to address all those? The second question is, there is a real challenge when trying to discover new materials. Firstly, you have got compositional space, but then you have got how you have synthesized it, the quality of the material. And you can synthesize things badly and then they can appear badly. And that is related to also how you assess the material, and how you are characterizing these billion samples on a 2 by 2 cm substrate. Is this aspirational or do you have methods that you characterize these materials with already?

Chad Mirkin:

To me, there are three silos that are being built. One is synthesis: what can we make? Two is screening: what are the structures that are active, what are they actually doing? And the third is data collection and using that to train machine-learning and artificial intelligence. So we kind of work on building-up all three of those up in parallel. Remember that everything is position encoded. So, each feature is a discrete material, that is a big difference with the inkjet type synthesis, which people often refer to as *spray and pray*. In thin films, where you got a lot of heterogeneity, every site is a single particle of a fixed composition. How do you get that? The commercial print heads have 160000 elastomeric tips, all nanoscopic in terms of sharpness. They are uniform, that is something that we worked out over the last decade in half. We spray a precursor on those arrays, that varies in composition, from left to right. So, when you do that, every tip is printing a reactor that has a different set of precursors. These elastomeric tips are compressible. In the instruments, if you tilt them, the left side comes down first and makes big features, because the tips compress. The middle makes some medium features, and the right side makes very tiny features. So, in one shot, you can not only make 160000 different features with respect to composition, but different with respect to size. That takes a fraction of a second, to make the precursors. Do it over-and-over-and-over-again. That is how you get to millions and billions very quickly. And then, everything is processed in one shot and converted into particles. So, all the different reactors have different volumes and different numbers in ratios of elements, but they got fixed positions. And now, you screen, and you collect your information. You look at where do we have activity — we are choosing to use electrocatalysis as the main driver with calorimetric indicators

to tell us where we have hotspots. And then we go in and do exactly what you said. If this is a hotspot, we go in and structurally characterize that and understand whether it is a discrete particle, or was it an error — because that would be a problem. And if it is a discrete particle, we are now at 95% being particles that are fully intact. What is the composition? How is it presented? Making it many times over to see if we can make it over-and-over-and-over-again to create structures that exhibit qualitatively and quantitatively similar properties. But it is a challenge, and it is one that we have been working on, but there is a lot going on. There is a company called Stoicheia that we started, and a big investment is being made in this space, for obvious reasons. This is a way to look at materials really, really, fast, and we think it is going to yield some winners pretty early in the process.

Omar Yaghi:
I just have a follow up from Henry Snaith's question. Are you making compounds? What I mean by that, a compound has a well-defined composition. The things that you are making, are they compounds? And if they are, what are the chemical formulas?

Chad Mirkin:
It depends upon the materials that we are looking. In case of the halide perovskites, we are definitely making compounds, with well-defined compositions, ratios, and structures. They are characterized at the X-ray level. In the case of the particles, the heterostructures, those are alloys and heterostructures that consist of different domains that have been merged together. And in many respects, it is kind of interesting they even form, because you could imagine a situation where instead of forming one particle with four different phases all merged together, they could form four different particles. But the conditions of the experiment typically drive all of them together, as I showed in the 7-element library.

Omar Yaghi:
If these alloys, are not compounds, then how can they be reproduced? Or do you mean you do know the exact ratios of those? I am having trouble understanding how these compositions can be reproduced, like the alloys that you just mentioned.

Chad Mirkin:

The thing about molecular chemistry is that I can make a mole of molecules, where in principle every molecule is the same. With particles above a certain length scale, I cannot make a mole of particles where two particles are the same. So, there is an average structure, defined by composition and general phase, and that is how they are characterized, identified, and reproduced. But I would have to tell you that, for the vast majority of the catalysis, that is what we work with, what we identify, that is what we run with. The molecular approaches try to replace that, to use precision to exceed that capability. But in many cases it does not work, because you cannot work under the conditions that are relevant. Or it does work, and you find routes to go down that particular path.

Omar Yaghi:

I guess my question is, if they are not compounds, then how do you calculate the yield at the end?

Chad Mirkin:

You define an acceptable set of parameters. Just like in any heterogeneous material, you define what is an acceptable product, based upon general size. What is the dispersity, greater or less than 10%? What is the elemental ratio? How far does it deviate from that? You define, as the user, what is acceptable. And you can drive yourself nuts with it. If you drive it down to an individual atom, you know, you will never get to an ability to make structures of interest. But the good news in this space: for a lot of the materials that are very useful, average structure and control over many of these parameters, within the set of possibilities, gives you the ability to make materials exhibit generally reproducible properties and properties can be used, especially in the area of catalysis.

Nicholas Turner:

Continuing the application theme, several of the speakers discussed the encapsulation of proteins, including enzymes, in MOFs, COFs, metal peptide frameworks, which I found very interesting. So I started to think about what would be the sort of advantages or also some of the challenges in putting enzymes inside some of these frameworks. Stability, I can imagine a protein would be stabilized by encapsulation, that would be

advantage. Porosity, I think is interesting, because when you immobilize enzymes, they are often mass transport limited depending upon the immobilization and encapsulation method used, so that could be interesting. Separation is an obvious one, you might want to have enhanced separation technology. Leaching or lack of leaching, which was mentioned earlier, is very important. If you make pharmaceuticals and if you use a biocatalyst in the last or penultimate step, it is very important that you establish rigorously that there is no protein component in the API, for obvious reasons. I wondered just to finish off, whether you could encapsulate two different enzymes within a MOF? I do not quite understand how you do this, but I would be very interested to know. If that is possible, then one can imagine building encapsulated cascades, potentially. I would appreciate any feedback or comments on any of those questions.

Makoto Fujita:

The encapsulation or spatial isolation of proteins is a very interesting and challenging topic in both MOF chemistry and in our cage chemistry. So, let us think about the instability of proteins. Proteins often easily denature, unfold. But most of the degradation steps initiate through the aggregation of proteins. Finally, it precipitates. It is always a major pathway of the degradation of proteins. Once the protein is isolated, so physically isolated, they have no opportunities to aggregate with each other, then the protein will be remarkably stabilized. Maybe the same phenomena were observed both in MOF chemistry and in the cage chemistry. Regarding a previous question, there are several examples of wrapping proteins by polymer matrices. But the proteins are too much biased and enzymatic activities significantly changed, reduced. But so far as we experienced, its chemical nature, including the enzymatic activity, does not change while it becomes very stable because their aggregation is completely prevented.

Xiaodong Zou:

It is possible to immobilize more than one enzyme in the pores. There are MOF materials with different types of cages, and you can first immobilize the larger enzymes, and then the next step is to immobilize the smaller enzymes into the smaller pores.

Chad Mirkin:

In the case of DNA, it is actually trivial and done. You can take almost any protein and modify the periphery with oligonucleotides, and use the same design rules and program crystallization. In fact, you can get higher quality crystals than you get with the particles, because the subunits are molecularly pure.

This idea of building cascades: we have done as many as five different proteins and multiple different enzymes within one structure, and that is the exact direction that this is all headed in. Controlling protein crystallization, where you do not pray for a particular crystal, but you guide its outcome based upon these design rules.

Yamuna Krishnan:

I was interested in why you chose to describe the DNA duplex connecting two entities as a bond, rather than as a linker, because in my view, bonds are a subset of linkers, that it is every bond is a linkage, but every linkage need not be a bond. So I was just wondering, if you could expand on that?

Chad Mirkin:

It is a really good question. We wrote a review on the whole area because we cannot view each other going down this path with very different sets of principles, and he asked the same thing. I said the reason is, when we make these constructs, density is critical. We do not use a single oligonucleotide as a linker. If you recall, Paul Alivisatos did work where he kind of aligned particles on a DNA template. I call that linking, to me that is a labeling, it is very similar to labeling with a fluorophore. In this particular case, the density is critical. We load up the oligonucleotide on the surface of the particle, so the oligonucleotides were forced to stand upright and adopt the directionality imposed by the particle core. That leads to true bonding characteristics. That allows you to get valency, when you go from a sphere to a cube, to get an octahedral type of arrangement, trigonal prismatic. It allows you to dictate architecture in a way where you can predict ahead-of-time bond lengths. If the oligonucleotides are floppy and allowed to all move and sample space in different directions, then you have no predictability in terms of bond length. Here, if I want to adjust bond length, every base I will add 2.6 Angströms of distance between the

particles. It is perfectly linear, over really large distances. So, I truly believe in the context of these types of constructs where the oligonucleotide are loaded, the appropriate analysis here is a type of bonding. It is a bonding that we take advantage of, and this idea that bonding is independent of atom identity gives you the design space that I have tried to articulate.

Yamuna Krishnan:
Prior to today, my understanding of a bond was something where the length, the angle, and in fact the covalent character, was set by the quantum mechanical descriptions of the atoms involved on either side of that bond. So, you are saying that we should now kind of free our mind of that construct, of how we perceive bonds?

Chad Mirkin:
Let us say, expand it. What do you think of the mechanical bond? There are many types of bonding. We are expanding the definition of bonding and how you ultimately use it.

Omar Yaghi:
I think the question is: is a DNA linker a bond? I think chemists are very fussy about what a bond is. And even the mechanical bond is an entanglement, and I agree it does not have a quantum mechanical description. So I think that the source of this question is: should a DNA strip be called a bond because it links two things together? How about we ask Professor Sauer?

Joachim Sauer:
First of all, I do not understand this. Can you explain me how is the DNA interacting with these things you are connecting?

Chad Mirkin:
In this type of situation, you have particles, they are not atoms. We call them atom equivalents and if you want you can call the bonds between them bonding equivalents. These particles are loaded up with oligonucleotides with sticky ends, so stretches of bases, single strands that can define

the recognition properties of the particle with respect to other particles. There is directionality imposed on the bond identity, the oligonucleotide in this case, because of the density of the oligonucleotides on the particle surface. And when you use these types of constructs in this way, you can begin to build matter, as I have said, that spans an incredible amount of phase space, where you can control lattice parameter, which we typically associate with bonding, with sub-nanometer resolution, over very large length scales, and you can realize crystal symmetries that have mineral equivalents and ones that do not. Finally, you can drive to specific crystal habits, because thermodynamically what is favored in this particular case, is to maximize bonding or pairing, oligonucleotide pairing. And so those principles allow us to make the equivalent of molecules and materials, crystalline materials, in a way that people have not done before.

Joachim Sauer:
I know that I am entering difficult territory, but would it not be a supramolecular arrangement?

Chad Mirkin:
Not a doubt. It depends on the way you look at it. We used the chemistry metaphor in this case, the model, as a strawman, to say what we can do with particles as atoms and oligonucleotides as bonds that we do with conventional chemistry, where do we fall short, and where can we go beyond. And that has been kind of the framework of developing this field for the last 30 years, and it has proven pretty useful.

Omar Yaghi:
I think that the source of the confusion is that the chemical bond derives its attributes from the atoms that it links, and I think that the people who are sticklers for this, probably are saying: "Hey look, there is a strip of DNA, and it does not matter what stuff you have linking, on either end". I think that is probably the source of the question.

Chad Mirkin:
That is why I started up by saying it is the advantage that it is independent of atom identity, so nobody is calling this an electron bond.

Omar Yaghi:
I think then it should be called a linker, because I could call terephthalic acid that is linking two clusters, a bond.

Chad Mirkin:
If you get directionality, yes.

Omar Yaghi:
It certainly does.

Kurt Wüthrich:
I have a comment to the question by Nicolas Turner. In my field, we have used inverted micelles to suspend functional enzymes in aqueous solution in a low-viscosity organic solvent, just to improve the quality of the NMR spectra. In spite of the very specialized use, I think it relates here to the kind of encaging that you all are talking about.

Arne Thomas:
In short, this is exactly what you said, you suggested. Everything was totally right about what are the advantages of immobilizing enzymes into MOFs or COFs materials. Then you said there might be also coupling, and also this has been done, using two different enzymes, as Xiaodong Zou said. But I think you can have a little bit more fantasy there and think of why just coupling two enzymes. You can also probably couple an artificial catalyst with an enzyme. And then, because we can compartmentalize the whole thing — Omar Yaghi got this idea of actually separating gas molecules — we can probably also separate solvent streams, so that you have one compartment where an enzyme can work with an organic catalyst that should work in an organic solvent that would normally kill the enzyme. We can actually have different compartments of a COF or MOF do different kind of catalysis and then transfer products to make a real cascade. Because this is a big problem, yesterday cascade catalysis was mentioned. For two catalysts working together for cascade catalysis, always all conditions have to be exactly working together: temperature, solvent, and so on. I have at least the hope, this is not done so far, but I have the hope that one day we will be able to do this in one material.

Ben Feringa:
I hear a lot of interesting discussions about templating and precise organization. As far as I know, for decades, people have tried to imprint in polymers, sticklers, to do polymer imprinting, like for instance a transition state for a catalytic reaction. As far as I know, they have not met with much success at all. Should we revisit this field, using your approaches, and getting real imprinted, for selectivity, for separation technology, for catalysis, all these kind of things, using your approach?

Omar Yaghi:
I will give you a free idea: I think you can evolve. The multivariable systems are really fascinating, because when you take a dumb crystal that is not multivariable, and put it in a soup of linkers that are differently functionalized, you may be able to evolve a structure around your substrate. And after you have evolved it several times, several generations, you may have the best imprint for that substrate. I think that is one way to do it. I do not like the term templating from MOFs and COFs, because they are really being put together by those linkages, they are very directional, and the stuff in the middle does not seem to matter; it is just space-filling rather than templating. I like to think of templating as something substrate specific for the assembly of a specific MOF, and we do not see that.

Ben Feringa:
That is what I would like to hear from you, because in the traditional polymer synthesis, there was hardly any success with this approach because apparently the dynamics, the reconfiguration, the adaptive behavior was not there, but here there seems to be opportunities.

Omar Yaghi:
Yes, because the backbone is rigid, and then functionalities are the ones that are shaping.

Makoto Fujita:
We have once tried the guest-induced assembly of its own optimal receptor structure from a mixture of several different ligands. There is a complex mixture of the metal and just several ligands, but by adding specific

template molecules, its optimal receptor structure would be predominantly assembled. We also tried to template with transition-state-like molecules, but unfortunately, we have not obtained good results. We actually tried to do that imprinting in our self-assembly system.

Stefan Lutz:
I want to follow up on Nicolas Turner's question about proteins in MOFs and COFs. Two parts. I would be curious about electron transfer. If you encapsulate an enzyme or protein in your type of arrangements, you showed the very nice example with the nickel catalyst, could this also work for the entire protein? And then thinking along the lines of just the last comment, talking about the evolvable container, but of course the protein can also be evolved to work optimally in that container, so here you are now looking at a system that can be improved in two dimensions. I would love to hear your thoughts.

Arne Thomas:
The first answer is yes, this we know already. I will not tell you too much about it, but it is working. You can encapsulate enzymes and you make an electron transfer, photo-catalytically or electro-catalytically. This is both working. It is a bit of a question, and now we come to the difficulties, and you know these of course. The question is how the electron transfer occurs. It is a little bit the orientation of protein and so on. So, there are many things happening in three-dimensional pores and the question is: from where is the electron coming? I cannot answer for the moment, but I can tell you it is working.

Regarding the evolvable container, this is actually the same answer more or less, as the question is: how it orients? I think we have many opportunities, because we can change, and this is always what I say with this multifunction and multivariate thing. You cannot change only such that we optimize electron transport, but also the polarity, for example, this might be superb. This is extremely important, I think, to evolve the protein there. Should the protein really stick to the surface, because it is hydrophilic and has hydroxy functionality? Should it be a little bit more apolar, so that it stays more within the cavity, but not attached to the support too much? These are things we are trying at this moment to find out. The last

example, you have shown there was something where we can gradually change polarity of this type of COF materials, and this is something that I think will be very interesting, to see what the protein in such pores is doing. Again, with this notation I made in the beginning: do not change three things at once, because then you do not know what the effect is. Try actually to stick to one material, but gradually change one parameter, like polarity, and see what protein is doing in there.

Karthish Manthiram:

I think it is brilliant to see structure at such a fine scale. Xiaodong Zou, as you described it, it is very remarkable to be able to pick up these minor phases that we would otherwise be blind to. And I think, as you implied, these minor phases in many cases are probably, or could be, responsible for catalysis. I just want to get your take on to what extent do you foresee this possibility to be able to map catalytic activity at that fine length scale, at this tens of nanometer length scale, so you can now correlate these maps of catalytic activity with the phase behavior, this heterogeneity in phase behavior that you see, and bring those two together?

Chad Mirkin:

I think that's where it is definitely ultimately headed to. But you know you have to start a new area. Start talking about things as DNA bonds. You have to think about how you do navigate in that area in a way that allows you to do biggest things first. So you are talking about something that is really, really important, and will undoubtedly be an issue of interest, but it is not the big ticket item from the start. The question is: can you use this to find things, first of all, that do what we need, that we are all excited about, and then use redundancy and the ability to duplicate many times over to explore that to the level that you need to get to the point where you can scale up and use it for that particular purpose? If that demands that we understand that architecture down to the individual atom level, then we got a much higher challenge or higher bar for us. In many cases, it will not, I am convinced of that, but we will eventually use this as a tool to get better and better doing this. I have one student who is taking it down to making particles that are 1 nm in size. It is a countable number of atoms in the cluster. It changes how we characterize. We are having to use

aberration-corrected electron microscopes to characterize these types of structures. Challenges in terms of characterization go way up. This is all part of the whole evolution, I think, of this particular area, but initially we are going in with the brute force approach. Let us take what we can control today, elemental composition, size, define parameters and acceptable variances, build those libraries, and see if we can find things that do what we cannot with conventional materials. So far, we found a few, and we are going to find a lot more.

Xiaodong Zou:
I would like to say that now, with electron crystallography, it is possible to really both see the materials and also determine the structure, and understand the detailed structure at the atomic level. And also most importantly, you can study the heterogeneities, which means that you can have a complex material or a material with different components, and it is possible to study it. So, I would like to think of how that would change the current way of making materials. Because you are thinking about the simple components and trying to get a big crystal and pure materials, but what if you put many components and molecules together and see what you get? And also, being able to look at the evolution of materials in different environments, and the catalysis, while we can both see and know the structure with atomic precision.

Chad Mirkin:
I just think it has become a necessity that people like you come up with high-throughput ways of characterization. Characterizing one versus 225 million are two different issues. So, figuring out how you get structural information on the things that matter is going to be a big part of how this either moves or does not move going forward.

Xiaodong Zou:
This is a challenge, and we are moving towards that field.

Matthew Kanan:
My question is with respect to catalysis. I guess the way I see what you are able to do, is you can control the functionality in the individual spaces inside these materials pores, and then you can create a distribution of

combinations of those functionalities, which you are calling multivariate materials. I am trying to understand the added capabilities there a little bit better. Obviously, the functionality within a certain space is what makes zeolites special. They have very acidic sites, they have pore sizes that interact with hydrocarbon substrates, and they are thermally stable, and that is the magic of zeolites. Your new materials, you are, sort of, in a different temperature regime, and you can decorate, I suppose, with more functionality. But is there an example of a catalytic transformation that you can perform, based on your ability to position three or four different functional groups that are important, that cannot be performed with a molecular catalyst that is tailored to that specific transformation?

And the second question is that, I guess, I still do not quite see the power of it. If I have a substrate coming in and it sees one environment, that maybe catalyzes a reaction of that substrate at a certain configuration, and it is going to diffuse over to the next pore that has a different configuration. I do not understand how that works, unless it happens to be that ABCD vs DCBA, that those two configurations give you sequentially two transformations, which seems to be rather unusual circumstances. I am missing the power of having that variability. You both sort of alluded to this sort of cascades and these networks, and I guess it would just help to have an example to understand how one can do that, as opposed to lots of great technologies for immobilizing enzymes and solid supports to be amenable to high-throughput synthesis. There are ways of encapsulating and protecting things. I am just trying to understand the power of ordering in these three-dimensional spaces, or sampling large heterogeneous mixtures of configurations of functionality a little bit better.

Omar Yaghi:

Molecular chemists spend their lifetime trying to organize ligands around a metal for a specific transformation. There has been a lot of time perfecting that catalytic pocket, if you want to call it that. What my thinking from multivariate was is to introduce those ligands that a molecular chemist would, although the molecular chemist has to also do protections and things like that, that you do not have to do in the MOF because the MOF is a protecting group. Let us take the TEV protease enzyme example that I gave. We just introduced the amino acids that we thought approximate

the pocket into the pore, and we build a short peptide of four amino acids, one amino acid at a time. So the pore is really internally heterogeneous and my thinking is that the reason the MOF, with all that lack of preplanning, still broke that specific amide bond that the enzymes did, is because it has billions and billions of microenvironments and a certain, perhaps small, fraction of them is fertile for that particular selective bond cleavage. The rest of them are inert to that transformation. The problem of course of this approach is that, while a molecular chemist does things with precision around the metal, in this one you are throwing everything in there and saying: "Hey, instead of making one complex, I will make billions of microenvironments, billions of complexes and just let the substrate sort of find its way through". The problem, ultimately, that you have to reckon with is, what are those environments that are fertile? And the second thing, will the substrate after transformation be able to diffuse in and out easily, with all that stuff that is happening in the pore? So, there is a lot of stuff you have to do to make sure that it follows the logic of molecular chemistry. But I feel that it is an opportunity to sample a combinatorial set up space within the crystal. This was my idea about the fact that we do not know what these sequences are, we need to figure out a way of doing that.

Matthew Kanan:
Maybe I just misunderstood. The combinatorial space is the different functionalized linkers. How many different functionalities are you putting in one of these?

Omar Yaghi:
I think there are seven reactions that are leading to a short peptide of four amino acids, and each transformation is not 100% complete. So, you have really a forest of one amino acid, two amino acids, three amino acids, four amino acids, and it is just everything is in there. It is not a clean environment, but nevertheless it did these transformations.

Matthew Kanan:
And based on the kinetics, can you estimate different possibilities of what fractions of those sites are active?

Omar Yaghi:
Hard to say. We just know that there was, I think, 70% yield in terms of the cleavage.

Karen Goldberg:
Have you ever in these MOFs used the ligand in a metal-ligand cooperation, in terms of using the metal center and the ligand within the MOF? So, using the metal as a catalytic center? Because you are using ligands, but a site of ligand could cooperate with the metal in terms of doing a bond activation.

Arne Thomas:
This has been done many times. You can actually make MOFs with open sites. In some MOFs, some middle sites are fully coordinated and they are not active in catalysis anymore, but you can create MOFs with open metal sites, and then the metal site itself can be catalytically active, and you can use the linker for another incorporation of metals. This has been done, even though I do not have the application in mind, which kind of catalysis it was.

Omar Yaghi:
Ok, we have come to the end of the discussion. We had a great discussion, thank you, thanks everybody.