

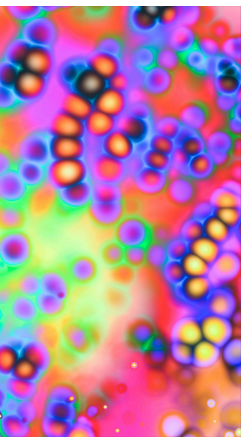
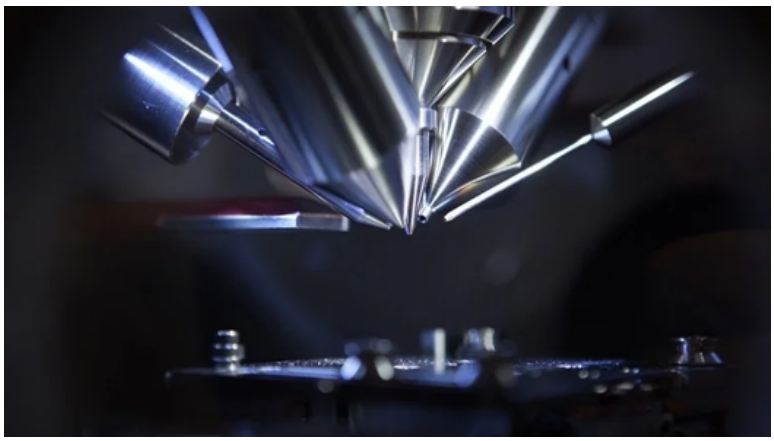
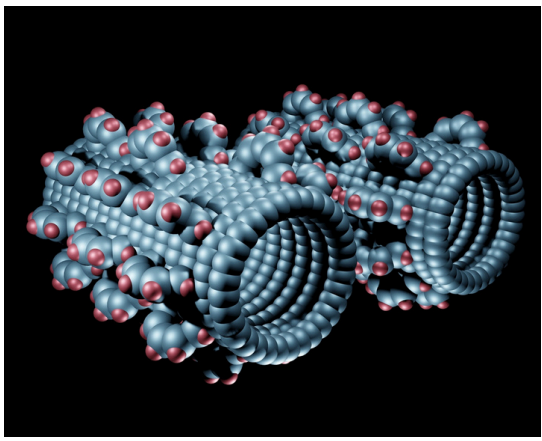

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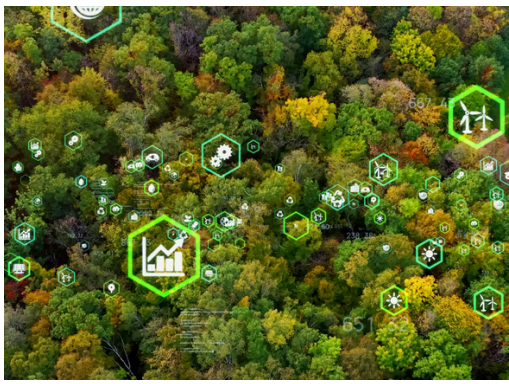

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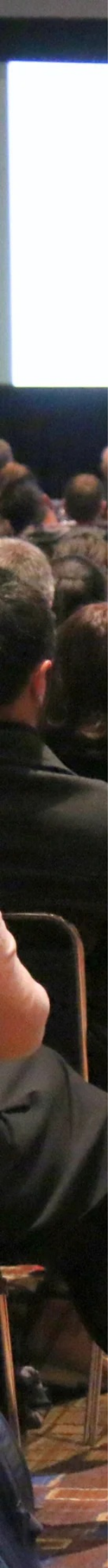

Tackling healthcare challenges in a changing world: an interview with Professor Jeremy Nicholson

What is the exposome and how do the changing interactions of human genes, microbial genes, diet, lifestyle and environment all contribute to shifting patterns of disease?

As individuals and as populations our risks of getting diseases are determined partly genetically and partly from the environment that we live in. An important part of that environment that mediates between the outside world and the inside world of our bodies is the microbiome.

Our guts are filled with bugs. There's up to a kilogram of bugs inside you, with a collection of about 10 million genes. The human body has about 10 trillion cells, and the microbiome is about 100 trillion organisms living inside you at any one time.

The “exposome” is a concept that involves thinking about all the things from the environment that get into your body. It relates to your diet and to the microbes in your gut, which process the diet and make molecules of their own - microbial metabolites. Thus the “exposome” is the measured sum of the environmental exposures.

We also need to take into account the drugs we take, the chemicals that we're exposed to in the environment, together these exposures, plus your genes, determine your disease risk as an individual.

The exposome is all the different exposures that impact on the function of your body. The genome, the genes that you have, are really just the instructions.

Genes are just a set of instructions for building an organism in a certain way, and how that organism is built is determined by not only the program, the genes, the genome that runs it, but also the substrates that are available to it through the diet and microbial signaling from the gut.

Ultimately, our risk of getting a disease is highly dependent on all of those interactions. The other thing that's complicated about this is that the interactions vary throughout life, so exposures to diet variation, drugs, etc., that occur in babies have very different effects to the same source of exposures that occur in adult life, so there's a sort of conditional interaction between your genes and your environment that progresses throughout life, changing the risks for disease at any stage of life and the risks for getting diseases in the future.

In particular, probably the most important exposures, the most important interactions, are those in the first few years of life, where your body is programmed for a lot of the later biology that it's going to experience.

It's interesting to note that the microbiome takes about 3 years to develop, because babies are born without microbes and the microbes develop very, very quickly. In fact, there's trillions of bacteria within a few days of the baby being born, and it takes about 3 years before you get an ecology in the child that is similar to that of an adult, and so anything that upsets that development of the ecology in early life can be quite influential for risk factors later on.

How important is the microbiome in human health and why are disorders of the gut microbiome associated with multiple non-infectious diseases?

It's only recently we've started to understand how complex the microbiome is and how important it is to us. A lot of the bacteria that live inside us are not readily culturable, so microbiologists have only known a little bit about the biology of the microbes historically, because you simply can't dig many of the bugs out and actually make them grow. The reason for that is that these microbes live in an environment which has other microbes, different species in and they all work together and need each other.

Modern genomics and the technologies that were originally developed for the Human Genome Project can also be used for microbiome sequencing. About 10 or maybe 15 years ago people started to use modern gene-sequencing technology, so going into detail as to what was in this microbial community to find out who was there.

Now we know that there are probably 2 to 3,000 species in the human gut. It will vary between different people, but those 2 to 3,000 aren't the same species in different human individuals, so there might be bugs that are in you that are not in me and vice versa.

If you think about that in terms of genetic diversity, humans, you and I, say, are 99.99% similar genetically. Our microbiomes are probably less than 5% similar genetically. As we have an amazing microbiological genetic diversity within us and because the microbes perform a lot of biological functions for the human, which means that that functional variability is enormous between individuals as well.

To give you an idea of what I mean by function: there are biological pathways that control our body, a lot of them are under the host genetic control. For example, the enzymatic sequence for breaking down sugar, glucose down into smaller bits that can be used for energy metabolism, is under human genetic control.

There's lots of other pieces that are biochemical machinery in the body that's not actually under human genetic control. In fact, quite a lot of cholesterol metabolism, for instance. People talk about cholesterol a lot, the good cholesterol, bad cholesterol, but in fact, if you look at the cholesterol pathway, the conversions from

all the different metabolites, the different sequential chemical conversions, and cholesterol metabolism leads to steroid metabolism, etc., these are highly related.

Something like 90% of all the conversions in those pathways are partly determined by microbe-signaling molecules. If you like, some fundamental parts of our own machinery are controlled by microbial activity. Microbes make compounds which are drug-like, they switch on and off our pathways, and it's only been recently understood just how deep that connectivity is, and this is the basis of what biologists call symbiosis.

Symbiosis is about 2 or more organisms that are physiologically connected together, and they perform functions for each other, resulting ultimately in a situation where one cannot do without the other, extreme examples of symbiosis that organisms cannot survive without each other.

Humans can survive, just about, without their microbes but they don't do very well at all, and in fact all animals with a gut rely on their gut microbes performing a lot of biochemical functions, as a result of which they exhibit "genome reduction."

Genome reduction is actually a reduction in your own number of genes because you've got someone else to do the job for you. This is quite an interesting idea, because it means that humans are actually incomplete as an organism, they need microbes to make them complete, to control their pathways properly.

To give you an example, if you'd make gnotobiotic (germ-free) animals, e.g. by C-sectioning rats and keeping them in a germ-free environment so they never get exposed to microbes, the normal surface of the gut, the so-called villus surface of the gut in those rats never, ever develop.

The gut has got lots and lots of very complex surface area increasing invaginations and villi, little projections. The development of all of that anatomy is dependent on microbial signaling, so it's an extraordinary thing to say that your gut structure is not even encoded by your own genome.

It actually requires microbial genomes to make it work. That's just one rather splendid example of genome reduction, but the important thing is the diversity of the microbes.

If you can imagine that your biology is being partly controlled by microbes, your

microbes are different than mine, our biology is different because our microbes are different, and therefore the way that we interact with the exposome, the way we interact with diseases, the way that we respond to drugs, even, is dependent on variations that ultimately advance variations in our microbes.

We've only really started to understand just how deep that connection is in the last 5 to 10 years. If you can bring it back to humans, and things like understanding how drugs work in the body, drugs can be detoxified by microbes so they can make them less toxic, or they can be made more toxic by microbes, so there are some splendid examples.

Amphetamines are metabolized by gut microbes. Digoxin, the heart drug, is metabolized by microbes, so your different microbial composition changes how drugs work in you as well as the likelihood of diseases occurring in you.

When you think about this from the population level, the population disease risks change partly due to behavior of the people, what they eat and how they exercise, but also because of their microbes, but at the individual level drug therapy is changed by microbes as well.

When we come to personalized healthcare, just having the human genomic part of it is not good enough, because it doesn't explain a lot of the variation that we have physiologically between individuals, which we need to understand and optimize therapies for individuals.

The microbiome is going to be important in the future because it will help us understand disease risk, and the way that environment and the human body interact through the microbiome, but also in personalized healthcare we're going to have to understand the microbiome to get that fine tuning of therapeutic management that we're going to need in the future.

How does this complexity impact pharmacogenomics?

Pharmacogenomics has had few successes given the effort and money involved. You can certainly stratify people into different genetic classes of disease, breast cancer is a good example, where there are about 10 different genetic sub-varieties that you can detect, and some are more or less responsive to certain drugs.

If you know about the genetic backgrounds of somebody, you can start saying whether a particular drug is likely to be good for that person. There have been some successes there.

The point is, even within a specific genetic sub-classification, there's still quite a variety of patient variation and response to therapy. Some people respond better than others, and that extra variation has to do with things like your physiological variation, your microbial variation, your lifestyle variation.

If you put the genetic information together with the microbial, and sort of the metabolic phenotypes you can measure, you start to cover all of the bases and you end up having a much deeper understanding of human biology that you need for personalized healthcare.

What new technologies and systems have been developed to help us understand the complexity of human diseases?

Genomics has been tremendously important in helping us understand the basis of disease, but the fact of the matter is that most people in the world die of non-genetic causes; they die of environmental causes; they die of starvation; they die of infectious disease.

We need technologies that go beyond genes, and so people have developed technologies looking to proteins, which are the machines that are made on genetic instructions to run the body, and there are technologies for looking at metabolism, which is the small-molecule currency of the body, the energy balance, the breakdown of food, the excretion and the building and excretion of metabolic products that we don't need.

Each of those different areas requires different technologies, so each level of what we call "biomolecular organization," the genetic, the protein, the metabolic, requires a different type of technology to explore the variations in human biology.

Genes give you the potential of what might happen in relation to an environmental stimulus, or stressor. The proteins are the machines which execute the variation in the genes and the metabolites are the products that tell you what's actually happened in the body. Because the patterns reflect fundamental activities of the chemistry within the body, it often tells you why there's a problem as well.

Some of the most important technologies to be developed recently have to do with metabolic analyses, which allow you to do thousands and thousands of metabolites quickly and precisely, which gives you deep insight into human biology.

In what ways is our understanding still limited?

What we are challenged by is the number of levels of biological interaction and understanding what it means for the human. We think of this like the microbes playing a tune, a chemical tune. Microbes make molecules, which switch on and off receptors in our bodies and control pathways.

Another challenge is understanding all of these different microbes, all talking to each other and talking to us, and which ones are controlling the overall signaling process. We just simply don't understand that yet. When we do understand that, and we will eventually, then we'll be able to start making interventions in it.

If you imagine that a particular metabolic pathway in the human body is controlled by a molecule that's made by a microbe that can switch on and off, maybe a pathway in the body, if you switch it off you may change a disease-risk factor, a cancer or something like that. We think such things exist.

If you could understand which microbe was making which molecule, and you could work out then a way of switching off that microbial metabolite production, thus changing the activities in the human body, and then potentially changing a disease risk.

That's the big prize in the future. It's a whole new way of thinking about therapy for the human body by thinking of controlling microbial activity that exists within us as a way of controlling our bodies, and maybe even intervening in disease processes or preventing disease processes occurring at all.

Although our understanding is still highly limited because of the complexity, the value of understanding that long-term is going to be critical, because it will change the way that we look at medicine and the way that we develop therapies in the future.

What are the main challenges in personalized medicine and public health to date?

Understanding real human biological complexity in a way that you can do something about it. We talk a lot about “clinical actionability”, which is the ability for you to take certain pieces of scientific knowledge about a system or a person, and to be able to act on it so that the doctor who looks at this piece of information, says, "I know what to do next."

At the moment we have lots and lots of technologies describing human biology in ever more detail, but most of that detail is not very helpful to the doctor. He doesn't know how to use that to make a decision. The biggest challenges to personalized

healthcare is the translation of the knowledge of biological complexity into an actionable pathway that a doctor can use.

The same thing applies to public health where we are interested in understanding the basic causes of disease, whether they're genetic or environmental, and changes in disease patterns, and again it's about describing human biology in great detail, but at the population level rather than at the individual level.

We could also say that public health research exists to inform future healthcare policy. The challenge here is getting the biological knowledge and then expressing it in a way that it can be useful toward healthcare policy and also practically for giving advice to people as to how to run their lives.

How can we overcome challenges such as antibiotic resistance, obesity and physical inactivity?

Education is one part of it. The reason we've got antibiotic resistance is because we've misused antibiotics. The massive overuse of antibiotics in agriculture for increasing growth in cattle etc. has led to an environmental pool of antimicrobial resistance.

People didn't understand the long-term consequences of antimicrobial use for

agriculture. As a result we've got this environmental problem with microbial resistance.

Doctors over-prescribe antibiotics, and people often don't take a full course of antibiotics because they want to save some for later in case they get sick again, but of course the prescription is to destroy all of the bugs, the hostile bugs, and any that are left will be remaining because they're resistant to that drug.

We've ended up in a really very serious situation with antimicrobials and within the next decade there probably will be microbes that emerge that are resistant to all known antibiotics, and these could cause huge problems for the healthcare system.

We're already beginning to see it: 1 in 7 of hospital-acquired infections in the UK are non-treatable, and every person who gets an infectious complication in a hospital tends to increase their stay in hospital by 30%.

If you work that through, that's financially enormous. What we've got happening now is increased numbers of resistant bugs out there with new classes of drug resistance emerging, and so this problem is going to get worse and worse, such that unless something is done about it in the next 20 or 30 years, we will go back to 19th Century healthcare, where the majority of the population died of infectious diseases and not old age.

This is really quite an existential issue for modern society, and in fact there are some interesting angles one could take on that to do with the microbiome, which I'm going to come back to, but the same sort of thing applies to obesity.

Why are people obese? Well, they eat too much and they don't exercise enough. It's really standard, plain pharmacodynamics as a matter of fact. Why do they eat too much and not exercise enough? Because they're not educated properly to know that this will have huge impacts on their health longer term, and there tends to be associations between low socioeconomic status and obesity, and indeed low educational level and obesity.

It's not to say that poor people are stupid, not at all. It's because what tends to happen is that people are informed about healthcare according to their socioeconomic level, and also their ability to change their diet is determined by their socioeconomic level as well.

You'll find in any study on obesity that socioeconomic status, even salary, is correlated with obesity and things like that. Again, we've got to try and think about solutions that don't just work for the rich people but that also work for poorer people too.

Interestingly, of course, is the obesity epidemic that we're seeing now is partly related to changes in the microbiome, which brings us back to antibiotic use again. Microbes control a significant amount of calorific transfer from the diet to the body.

Quite a lot of your calories go into rebuilding the microbiome. There's 2 parts to it. Maybe 10% of your protein in your diet is actually related to building the microbes that live inside you because they turn over and you have to replenish those.

Another part of the protein in your diet goes to rebuilding the gut wall, because your gut wall turns over every few days as well, so that's sort of on the negative side, if you like, of the calorific balance that microbes take up calories because they need to build their own cells.

On the other hand, they also perform digestive and fermentation functions in the body, in the gut, which make more calories available, and so by changing which microbes are there you change the balance of power between negative and positive uses of calories, therefore potentially change the weight gain of an individual on a given diet. Understanding the microbiome is also important to understanding obesity as well in really quite complex ways.

Physical inactivity is a product of our modern lifestyle: we've got cars, we have fancy TVs, we like sitting around in front of them. A lot of people have sedentary jobs, where they're sitting in front of computers all day. That is a consequence of modern life, and people need to be educated as much as possible about healthy lifestyle and dietary choices.

Please can you give an overview of the MRC-NIHR National Phenome Centre? What are the main aims of the center with regards to metabolic phenotyping?

It came from the Olympic drug-testing center that was set up in 2012 to look at substances of abuse in athletes. It was a big analytical facility that looked at several hundred different substances that athletes might take to performance-enhance

themselves.

In 2011, early 2012, the Prime Minister was talking a lot about Olympic legacy, and justifying why we spent billions of Pounds on the Olympics, and what would we get out of it. People normally talk about swimming pools, sports stadiums and travel infrastructure.

At that time Professor Elliott, Head of Epidemiology at Imperial, and I wrote to Dame Sally Davies, Chief Medical Officer for England, and said, "Well, we've got a great idea for Olympic legacy.

Supposing at the end of the Olympic Games we take the Olympic drug-testing facility and repurpose it for a national facility for metabolic analysis for populations." We were in a very fortunate, very timely situation in making a suggestion that suited the politics of the MRC, the NIHR, and the government.

Then we were asked to write the grant proposal, which we did, 75 pages, some of it for justification by the peer review, and we were awarded 10 million Pounds by the MRC and NIHR, and we also raised about 11 million Pounds from industry to move the Olympic drug-testing facility into Imperial and create a national facility for large-scale phenotyping, which is what the National Phenome Centre is.

It's the first of its kind in the world and it's the only laboratory in the world that can do phenotyping at that scale. There's a lot of metabolic laboratories around the world but there are none of them that can do hundreds of thousands of samples a year, because the Olympic drug-testing facility was built for forensic-level analysis, because you're doing basically drug testing in people. If you get that wrong you're all over the newspapers!

We've built very high-quality control, a high throughput laboratory, that allows us to screen large epidemiological cohorts and populations to look for metabolic features associated with disease risks, as I mentioned obesity earlier.

The sort of questions are: what are the metabolic features of obesity that tell you about the gene environment interactions that precipitated the obesity? How does diet impact on your metabolism at the population level? Are there markers you can detect that predict cancer in individuals based on metabolic profiles? Are there markers you can get that predict stroke or cardiovascular disease?

The National Phenome Centre is a fantastic laboratory, and it's built on an industrial scale, and we're very lucky to have it here at Imperial. I'm currently involved in creating an international network of phenome centers, because now that we've built ours, lots of other countries want one as well. There's going to be ones in America, in Japan, China. There's already one in Singapore linked to Imperial and one in Birmingham has just opened too.

In the next few years there will be national phenome centers that will all use the same technology that we do, and harmonize our data so that we can all share and exchange information our population disease patterns, and so we'll be able to make the first on a global atlas of metabolic disease around the world by sharing our technology and data, which is only made possible by doing large-scale phenotyping studies.

The other part of that is the same technology can be used to doing patient profiling as well, so we can use it for personalized healthcare. We have a Clinical Phenome Centre as well in Imperial, which is funded by the National Institute of Health Research, NIHR, and then here we're not just looking at populations.

It will be individual responses to drug therapy as well, through the effects on metabolites so that we can record so that we know whether somebody is getting metabolically better or worse when they're under drug therapy.

How important are technologies such as NMR in research at the MRC-NIHR National Phenome Centre?

For metabolic phenotyping there are only 2 analytical technologies that are important: nuclear magnetic resonance spectroscopy and mass spectrometry. Both of these tools, these technologies, can measure hundreds or thousands of metabolites in any sample in the same analytical run.

They work in quite different ways. Mass spectrometry works on the molecular weight of molecules, the masses of them, how big they are and how they break up, how they fragment.

NMR looks at fundamental magnetic connectivity properties between atomic nuclei,

which are characteristic of individual molecules. They're complementary to each other. We screen every sample they get in the National Phenome Centre and our Clinical Phenome Centre by NMR spectroscopy in the first instance.

NMR gives us a good broad profile of maybe 1,000 different metabolites that are present in the samples. We get data, that's actually like a fingerprint, that's very useful. In things like blood plasma, we can measure all of the plasma lipoproteins quantitatively from NMR spectroscopy.

NMR is the definitive technology for measuring lipoproteins, and the HDL versus LDL balance tells you a lot about your heart disease risks, coronary artery disease etc. Intrinsically, NMR carries useful biological data.

There's lots of different sub-types of mass spectrometry. We use several different sub-types in the mass spectrometer according to the types of molecule we're interested. Now with mass spectrometry you have to do a bit more work.

You have to not only set right the sample using some chromatographic process, and then the mass spectrometer measures molecules individually and says what they are, but you can measure them more sensitively with mass spec, and you can measure more of them by mass spec than you can with NMR – maybe up to 25,000 metabolites.

What do you think the future holds for personalized medicine and surgery around the world?

Surgery is about the most personalized healthcare you can get, because it's one surgeon cutting you up, normally, so it's a one-on-one literally physical interaction. Of course, we're trying to revolutionize surgery by use of technology, so like the iKnife, which measures the chemistry of the smoke that's created when a surgeon cuts, and that can be analyzed using a mass spectrometer, so that almost instantaneously the surgeon knows what he's cutting through based on the chemical composition of the smoke.

There is a readout that basically does a mathematical analysis of the smoke chemistry in relation to a database where we have already annotated, if you like, the smoke chemistry. That's fantastic for personalization of surgery because it gives the surgeon more knowledge about the local biology of that patient to help in real time with the surgical procedure.

Of course, with personalized medicine more generally, when you look at maybe kinds of chemotherapy or other medical interventions rather than surgical ones, then metabolic phenotyping technologies give you much more detail about the individual variation in the biology of those patients.

We created a concept a few years ago called "Pharmacometabonomics," which is the metabolic equivalent of pharmacogenomics, where we use a pre-interventional metabolic signature and a mathematical model of it to say, "Well, you'll be this sort of person metabolically, therefore we know from experience that you're in this particular category, then we can potentially find which drugs will be good for you or bad for you." We've already demonstrated that with anticancer drugs you can predict efficacy and toxicity of the drugs in humans based on plasma metabolic profiles.

At the moment we're in this phase now trying to get into clinical trials for all these things, where we've got all these scientific observations, and we're now trying to create patient-journey clinical trials, so we really evaluate quantitatively how much improvement in healthcare we get by the deployment of these technologies.

Of course, we have to cost them in relation to care pathway as well, so in order to get the improved personalized healthcare and implement it properly in the healthcare systems, we actually have to improve people's health and shorten their journeys.

We have to save money in a healthcare system that's very strapped for cash, so there are 2 ways to save money in the healthcare system, really. Very basically it's, 1, spend less time in hospital when you're there, and, 2, go there less often.

At the moment it takes 3 or 4 or even 5 visits to a hospital for problems we've sorted out. What we'd like it to be is 1 or 2. 1 or 2 visits to the hospital, and then you're saving an enormous amount of time in the administration, etc.

Then the other thing is, if your hospital journey takes 5 days, can we improve treatment so it only takes 3 days, and not improve it from shortening the journey point, but actually have you better in a shorter period, but better for the patient, and you get that by doing personalized healthcare.

The more you understand the patient's problems, the more it's clinically actionable,

and you can intervene more quickly and effectively, which will help the patient recover quicker, hopefully improve the chances of their survival if it's a dangerous disease, or cancer, or something like that, and at the same time save money because it's shortening the journey.

If you can get all the components aligned, then the feature of personalized healthcare will be fantastic, but it's only going to work for certain disease areas. It won't work for everything, and one of the things that we're trying to do at the moment is to understand what is going to work for and what it's not going to work for.

Certainly cancer is an obvious area, because cancer is biologically, genetically, and physiologically quite diverse, so the technologies that we've been developing, which are about measuring diversity and variation in patients are going to be very useful, for instance, we think in personalized cancer therapies in the future.

We've got a lot of work still to do. We see light at the end of the tunnel, and what we've got to do hopefully is emerge from the tunnel before global warming or multiple antibiotic resistance get us, because those are looming up.

What do you think the future holds for antibiotic resistance?

Weaponizing the microbiome may be the way around antimicrobial resistance, because if we really understood our microbes well enough we could program them and to engineer them to destroy pathogens. That would be a much more effective solution than trying to invent a new antibiotics every 15 years and trying to do that forever, but we have a long long way to go!

Where can readers find more information?

http://www.imperial.ac.uk/phenome-centre

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- Faculty of Medicine, Imperial College London

Professor Nicholson obtained his BSc from Liverpool University (1977) and his PhD from London University (1980) in Biochemistry working on the application of analytical electron microscopy and the applications of energy dispersive X-Ray microanalysis in molecular toxicology and inorganic biochemistry. After several academic appointments at London University (School of Pharmacy and Birkbeck College, London, 1981-1991) he was appointed Professor of Biological Chemistry (1992).

In 1998 he moved to Imperial College London as Professor and Head of Biological Chemistry and subsequently Head of the Department of Biomolecular Medicine (2006) and Head of the Department of Surgery, Cancer and Interventional Medicine in 2009 where he runs a series of research programs in stratified medicine, molecular phenotyping and molecular systems biology.

In 2012 Nicholson became the Director of world's first National Phenome Centre specializing in large-scale molecular phenotyping and he also directs the Imperial Biomedical Research Centre Stratified medicine program and Clinical Phenome Centre. Nicholson is the author of over 700 peer-reviewed scientific papers and many other articles/patents on the development and application of novel spectroscopic and chemometric approaches to the investigation of metabolic systems failure, metabolome-wide association studies and pharmaocometabonomics. Nicholson is a Fellow of the Royal Society of Chemistry, The Royal College of Pathologists, The British Toxicological Society, The Royal Society of Biology and is a consultant to several pharmaceutical/healthcare companies.

He is a founder director of Metabometrix (incorporated 2001), an Imperial College spin-off company specializing in molecular phenotyping, clinical diagnostics and toxicological screening. Nicholson's research has been recognised by several

awards including: The Royal Society of Chemistry (RSC) Silver (1992) and Gold (1997) Medals for Analytical Chemistry; the Chromatographic Society Jubilee Silver Medal (1994); the Pfizer Prize for Chemical and Medicinal Technology (2002); the RSC medal for Chemical Biology (2003); the RSC Interdisciplinary Prize (2008) the RSC Theophilus Redwood Lectureship (2008); the Pfizer Global Research Prize for Chemistry (2006); the NIH Stars in Cancer and Nutrition Distinguished Lecturer (2010), the Semelweiss-Budapest Prize for Biomedicine (2010), The Warren Lecturer, Vanderbilt University (2015).

He is a Thomson-Reuters ISI Highly cited researcher (2014 and 2015, Pharmacology and Toxicology, WoS H index = 108). Professor Nicholson was elected as a Fellow of the UK Academy of Medical Sciences in 2010, elected Lifetime Honorary Member of the US Society of Toxicology in 2013, and Honorary Lifetime Member of the International Metabolomics society in 2013.

He holds honorary professorships at 12 Universities (including The Mayo Clinic, USA, University of New South Wales, Chinese Academy of Sciences, Wuhan and Dalian, Tsinghua University, Beijing and Shanghai Jiao Tong University, Nanyang Technological University Singapore. In 2014 was Elected as an Albert Einstein Professor of the Chinese Academy of Sciences.

Revolutionizing Glycobiology: A Mass Spectrometrist's Perspective

In this interview conducted at Pittcon 2023 in Philadelphia, Pennsylvania, we spoke to Professor Albert Heck and gained a mass spectrometrist's perspective on the field of glycobiology.

What is your professional background, and what first attracted you to the field that you work within?

My name is Albert Heck, and I am the chair in biomolecular mass spectrometry and proteomics at Utrecht University in the Netherlands. I am a mass spectrometrist with a broad interest in proteins.

By training, I am an analytical chemist but also a physical chemist and a biochemist. It is great that you can expand on what you are doing and cover all these areas from your basis as a mass spectrometrist.

How did your previous research prepare you for the field of glycobiology?

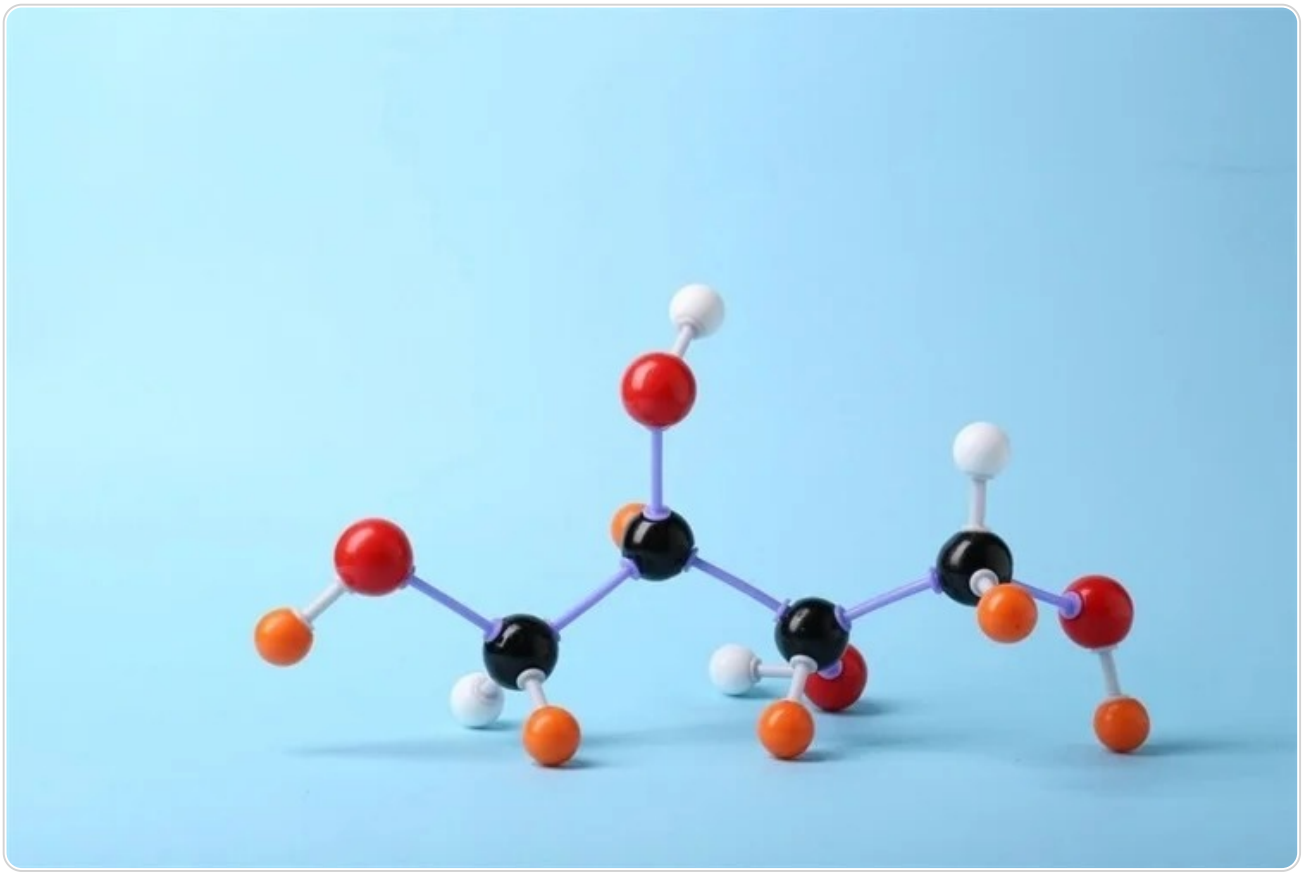
I worked for a long time on the analysis of proteins, and in the early days, we ignored that these proteins could also be glycosylated because it was too difficult to analyze. It makes the proteins way more complex because they are more heterogeneous.

However, through advances in mass spectrometry and analytical chemistry, we can now study these glycoproteins and the glycans that are present on glycoproteins, as have realized that these are crucial to their function.

If you really want to understand how proteins work, especially plasma proteins and proteins on the cell surface, you have to analyze and understand their protein glycosylation as well. I became interested in this field purely because I knew it was important.

What is glycobiology?

Biology is the study of life, but I do this more on the molecular level. I am particularly interested in how proteins work, and glycobiology is anything that is to do with sugars.



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> *Sugars can be free in your body and cells, but they can also be attached to lipids and proteins. They can even cover the whole cell with a sugar layer, which happens in most of our cells. The field of glycobiology is the study of what these glycans do, where they are, and what they do to protect us from all kinds of pathogens in the broader sense.*

Why is the study of the structure, the biosynthesis and biology of carbohydrates so important?

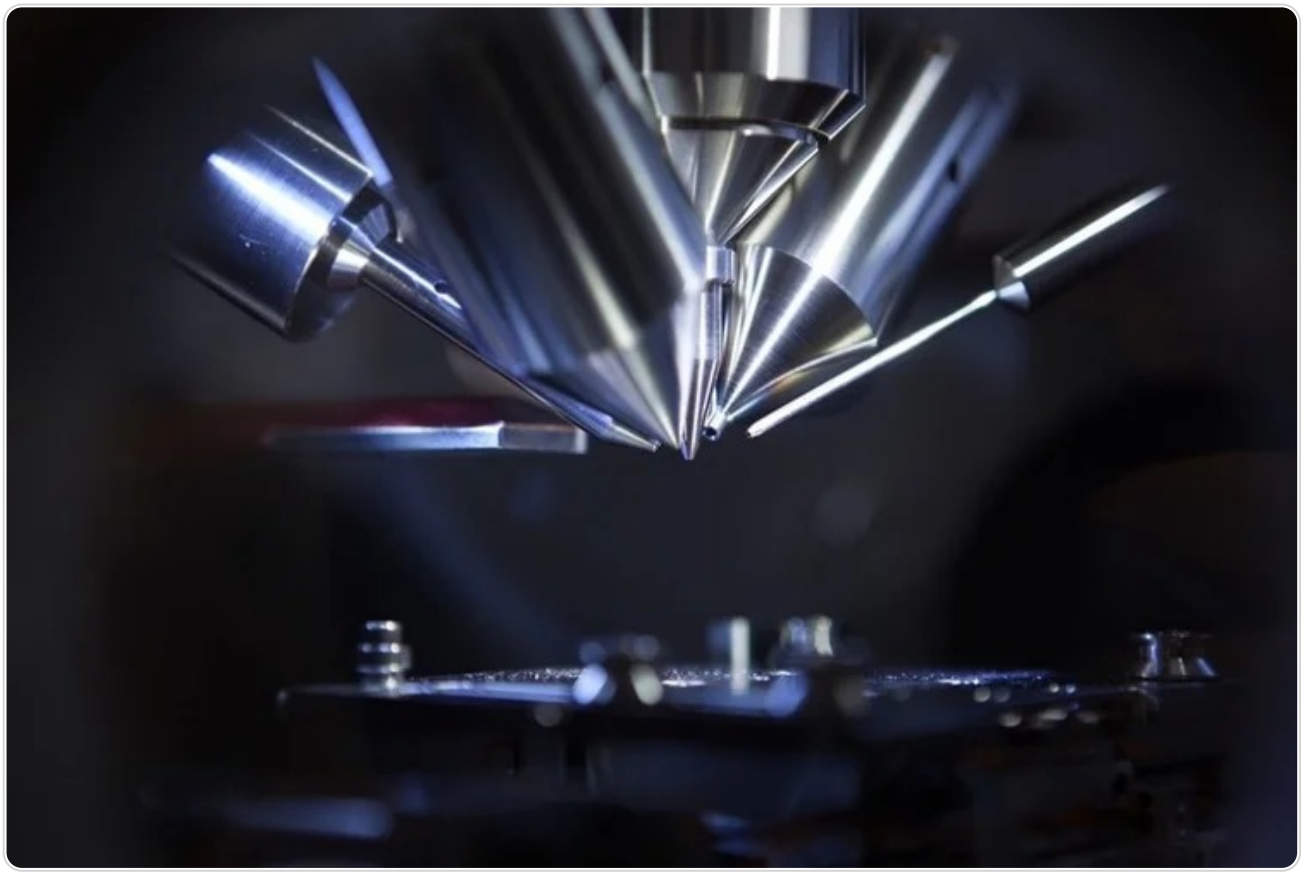
There are three stages when it comes to the study of sugars. Sugars that we typically call free sugars are, in scientific words, known as glycans. If these glycans are attached to lipids or proteins, we call them glycolipids or glycoproteins. It is crucial to study free glycans and how these glycans are attached to lipids or proteins, as they can modify the protein so that they can change their function and recognize each other. This can be both positive and negative.

For instance, if viruses want to enter our cells, they also have to recognize the glycans on the cell. If they recognize them, they can go in. If they do not recognize them, they cannot go in. This is just one, but very important, example.

How has mass spectrometry changed over the past few years, and how has this impacted glycobiology?

Mass spectrometry is a very powerful technique, and up to 10 years ago, it was pretty good at analyzing free sugars. However, when these sugars were attached to proteins it was much more of a challenge. In most glycoproteins, tens of different glycan structures can be attached to the protein, making the analysis of the structurally heterogeneous molecule much more complex.

With mass spectrometry, we did not have the separation yet to really define all the different glycan structures on the glycoprotein. But nowadays, with higher resolution, better separation technologies, better enrichment technologies, and better software, we became ready to enter this field, and are now playing an important part in it.



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Many glycobiologists that did not know mass spectrometry in the past are now using it for their analyses.

What are the main factors to consider when using mass spectrometry to study carbohydrates?

Carbohydrates are an immensely complex sample to analyze as they are very heterogeneous in their structures. They can also have different linkages that make them highly complex.

On the other hand, the human body has certain rules, and by studying how the glycans are attached to the proteins, we start to understand which glycans are put onto the proteins and their specific functions. Previously we ignored it, but if you really want to understand how life on earth works, you have to study the role of glycans on the proteins.

What are the drawbacks of current mass spectrometry models with regard to glycobiology, and how could those drawbacks be remedied?

There are always challenges; as mentioned before, we can measure masses, but we cannot easily measure structures. In the past, we used techniques like NMR and maybe even crystallography, but those techniques have limitations when it comes to studying glycans.

One of the weaknesses of mass spectrometry is that if we have two glycans that have the exact same mass but a unique structure because they have a distinct linkage of the chemical bonds, then it is harder for us to distinguish them.

The field is currently working on new techniques like ion mobility or spectroscopy to distinguish what we call isomers as they have the same mass. However, for now, using mass spectrometry in glycoproteomics is still considered a challenge.

What new approaches could be taken in the field of glycobiology?

There are many things being developed, and I think it is very interesting to follow the field of genome sequencing and the field of protein sequencing by nanopores. This highly attractive field could help overcome some of the previously mentioned challenges in the field of glycoproteomics.

At present, we cannot see how different isomers of a glycan or glycopeptide travel through a nanopore. Nanopore sequencing is still probably 5 to 10 years away from being developed, but it is an interesting field nonetheless.

New fragmentation techniques in mass spectrometry are also very important for

glycobiology and glycoproteomics. We work a lot on photon-induced fragmentation and electron-induced dissociation. These things have already emerged but still need to be developed further before being implicated in analyses.

What are the main challenges facing glycobiology over the next coming years?

The field of glycobiology is very important. We currently know that, for instance, the glycan shield on a tumor cell is different than on a healthy cell. But understanding this and how we can use this information to help develop therapeutics is one of the big challenges in the glycobiology field.

Over the last couple of years, everyone has become somewhat of an expert in virology. Yet, understanding how viruses enter cells depends on the glycan shield of the cell and the glycan layer on the virus. To understand that, we will need to conduct in-depth studies of these glycobiology aspects of almost every aspect of life.

How do you foresee your work in this field helping overcome such challenges?

> *You must always realize that your role in the field is just one out of thousands. I have been a mass spectrometrist for 20 years, and I have always been driven by my desire to show that mass spectrometry can always do more than what it could do yesterday. I am constantly looking for how this field can be further expanded and applied to new research questions.*

The field of glycobiology is so important, and there are still so many challenges to be overcome. In the coming years, we want to work primarily on the ability to better detect the masses of glycoproteins and glycoprotein complexes. We also want to be able to sequence them better and obtain better information on which glycans are attached to which protein under which physiological conditions.

However, there is still a lot of work to be done before we achieve this.

What are you currently working on right now that you are particularly excited about?

I am particularly excited about a technique that we developed a couple of years ago

where we made mass spectrometry way more sensitive; the technique is called single molecule mass spectrometry. We can also measure the masses of single particles and single molecules using this technique.

This single molecule detection technique can also be used to overcome some of the challenges previously discussed. This is especially true for molecules like glycoproteins that can be so heterogeneous that it is sometimes very difficult to measure their mass.

We developed the technology to determine the true sensitivity of mass spectrometry, and now that we have this in hand, especially in terms of the analysis of very large glycoproteins, we can see that its application is huge. This will be a highly beneficial technique in the field of glycoproteomics.

About Professor Albert Heck

Albert J.R. Heck (Utrecht University, The Netherlands) is scientific director of the Netherlands Proteomics Centre. Heck's group emphasizes on the development and applications of advanced mass spectrometry-based proteomics technologies. Heck introduced TiO2 and Ti4+-IMAC based technologies for phospho-enrichment. Heck pioneered the use of alternative proteases and hybrid peptide fragmentation techniques (e.g. EThcD, UVPD). His group also introduced 15N labeling in multicellular organisms and the cost-effective dimethyl labeling. Heck's proteomics research focuses for a large part on cancer, stem cells and immunology. Besides the proteomics efforts, the group of Heck is also well known for its expertise in mass spectrometry based structural biology, using native mass spectrometry, cross-linking and/or HD exchange mass spectrometry. The Heck-lab developed dedicated instruments for the analysis of intact proteins and protein complexes, with most recently a new high-mass Orbitrap, a serious breakthrough for top-down proteomics and native mass spectrometry. Through the development of the XlinkX and PhoX workflows they also facilitated proteome wide cross-linking studies. In recent years he has also focused on analyzing biopharmaceuticals, and plasma glycoproteins and immunoglobulins.

Heck is recipient of the HUPO Discovery Award (2013), and the Proteomics Pioneer Award from the European Proteomics Association (EuPA, 2014). In 2016 he received the ACS Field and Franklin Award. In 2014 he became elected member of EMBO and the Royal Netherlands Academy of Sciences and Arts (KNAW). In 2017 Heck received the

Spinoza Prize, the most distinguished scientific award in the Netherlands. In 2018 Heck received the Thomson medal of the International Mass Spectrometry Society and the Krebs medal (FEBS).

About Pittcon

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The Industrial Laboratory and the Changing World of Energy

In this interview, Dr. Joseph B. Powell, recently retired Chief Scientist - Chemical Engineering at Shell talks to AZoM about the past, present and future of the industrial laboratory for energy and chemicals which he will be presenting at Pittcon this year for the Wallace H. Coulter Lecture.

Can you begin by defining and describing an 'industrial laboratory'?

While perhaps less common than in the past, many companies have large laboratories where they develop new products and processes "in house". This is especially true for industries such as pharmaceuticals and specialty materials, the major automakers, semiconductor and microelectronics, and others where R&D is critical to development of differentiated technology and products. Fundamental science may also be explored to launch future opportunity, often in concert with external collaboration.

Shell has major R&D hubs in Houston, Amsterdam and Bangalore. These hubs include labs for small-scale bench experiments, as well as larger pilot plants and development units that are needed for scaling up processes. Industrial laboratories play a very important role in a company's mission to deliver new products and processes and to scale up to commercial deployment.

How essential is research into energy and chemicals, specifically analysis of its past, present and future, to the science and engineering industries?

It is very important because the world and society's needs are constantly changing and evolving. New and improved processes and products must constantly be developed to meet growing and emerging product and sustainability needs. Key issues today are climate change and the circular economy.

To effectively respond to these challenges, we must not only address the scientific targets and technical needs, but also how research is being done and how it can be performed more efficiently. To this end we look at how we are going about R&D and seek to continuously improve our methodologies and capabilities. This is very important for our goal of leading innovation in our industry, to meet the needs of our customers, stakeholders, and society at large.

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Could you describe the evolution of energy and chemicals research in an industrial lab setting?

In terms of actual pilot plant equipment, the Shell pilot plants from Emeryville dating back to the 1940s do not look that different from some of the units that we have today. And so, when it comes to piloting and scale-up, the process equipment itself often looks somewhat similar.

However, when it comes to R&D and some of the more advanced methodologies – for example, multi-throughput experimentation for catalysis, advanced in situ measurement devices and robotics for catalyst preparations – we have moved forward quite a bit in enhancing experimental capabilities. Instrumentation, automated control and data monitoring have progressed across all systems, and in the future we will see further automation of laboratories, as well as increased use of data analytics, computational modeling, machine learning, and artificial intelligence to improve efficiency and design. Being able to explore and develop more technologies at smaller laboratory scales with reduced footprint and increased safety, in shorter periods of time, is important.

Tell us about the importance of chemical and biological engineering in the context of everyday lives?

Tremendous challenges in energy and chemicals persist going forward, and chemical engineering will be at the very forefront of the search for solutions. Cell phones and their displays, your TV, laptop, video game console, smart watch, medicines and medical equipment, clothing and fabrics in your home, the cushion you sit on, the car, bus, or truck you use for travel or to bring you those on-line orders, virtually all features of what we now call everyday life are underpinned by materials and components that are designed and produced via chemical engineering.

Looking at and optimizing the process and industrial systems that are required and must be integrated into energy and chemicals, to do so necessitates chemical engineering. The plastics industry has been growing at roughly eight percent per year since 1950 and includes all of the products that you are using today that

comprise the "modern world".

The demand for new solutions remains high. Looking to the future, our industry must continue to address all stakeholder needs in providing products to you, the consumers at reduced environmental footprint, to protect the planet, its climate and resources.

You are going to be presenting the Wallace H. Coulter Lecture and your presentation will be titled, 'The Industrial Laboratory For Energy and Chemicals: Past, Present, and Future'. Tell us about what you are going to be presenting this year.

I will describe the pressing need to reduce carbon footprints to mitigate climate change, while meeting growing demand for energy and products which improve quality of life. The needed transition and transformation in energy and chemicals will require an unprecedented rate of new technology development. More efficient and effective ways of conducting R&D will be needed. I will explore some examples of the use of laboratory equipment and advanced methods to address these grand challenges and accelerate development and deployment of new technology.

AZoNetwork on Vimeo.

Could you tell us a little bit more about the challenges the energy industry is facing and how your research is going to help overcome those challenges?

Incorporation of renewable energy into the energy system and addressing issues like intermittency, low energy density and land use, are significant and important challenges. Electricity and hydrogen will play an increasing role in how energy is conveyed to end users. We need to further explore how we make use of bio-based or recycle feedstocks for synthesizing chemical products and fuels.

I will be addressing what those development programs look like, what the challenges are, and how core expertise in the fundamentals of chemical engineering and chemistry will provide a pathway to solution. Solutions to these problems must be found, and then developed and scaled up so that they can be deployed and used commercially. The energy industry knows how to design and implement the large-scale energy and chemical process systems that will be needed.

Your research covers novel chemical processes, oil recovery and biofuels. What are biofuels and their potential for solving energy challenges today?

Most people are familiar with ethanol biofuel, which is made by fermentation. For example, our Raizen business in Brazil is a world leader in providing ethanol from sugar cane to consumers.

I spent more than 10 years working on advanced biofuels, and Shell continues in these developments which take non-edible feedstocks such as food or plant wastes, agricultural residues, wood chips, or other landfill materials and convert them into fuels. Advanced biofuels would be drop-in replacements for conventional gasoline, diesel, or aviation fuels. No new infrastructure is required, but efficiency and sustainable conversion is a grand challenge!

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Energy and the environment have been intertwined by scientific research throughout the years, the latest concerns of energy regarding carbon economics. What advice do you offer for energy transitions to a net-zero carbon economy?

It is important to have a value or price on carbon so that we can move forward on addressing climate change and circularity and bring the technologies that we have been developing and progressing for decades into the marketplace.

If you look at places like Europe and California, there is some degree of carbon pricing and incentives now. This provides the impetus to bring hydrogen as a clean energy carrier into the marketplace, perhaps for driving fuel cell vehicles or converted back into electricity to power battery-electric cars.

How that is to be done on a major scale and become a dominant form of transportation and energy provides many exciting opportunities.

You have touched on how climate changes are a big factor for the energy community and energy applications. Your research covers energy and chemicals but also emphasizes sustainability development. How does the priority of sustainability shape the direction of your work?

I graduated from school during the energy crises of the '70s and '80s, when there was an absolute lack of energy. Gasoline was rationed, and there was high global anxiety about our collective future. Finding sources of energy for humankind was the overriding issue in "sustainability" for the day-- this was front page news!

Since then, we have discovered many different kinds of energy resources. The question has become which ones to use, where, and how, to address environmental stewardship, care for the planet, but also affordability so that access to energy is plausible for all people across the globe.

Stakeholders and consumers are increasingly asking for these aspects of sustainability to be added to the economic part of the equation, and that has been the focus of our new developments on energy and chemicals for the last few decades.

When I look back at our high-profile projects in the chemicals sector over the past three decades, these have been driven by delivering cleaner products to the marketplace, with processes that have a reduced environmental footprint. Shell formed its sustainability network in 1999 and I published a book on the subject, and this has been a major driver behind our innovation opportunities for multiple decades now.

In July 2020, you published “A hierarchical clustering decomposition algorithm for optimizing renewable power systems with storage”. Can you tell us more about this research?

Wallace H. Coulter Lecture

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I have to acknowledge some of my colleagues at the Energy Institute at Texas A&M

University for providing the high-level mathematics for that study, which deals with the intermittency of renewable energy. When trying to optimize and look at an energy system with high degrees of intermittency and complexity, it is very computationally intensive.

That particular paper described a new algorithm for the grouping of representative days of solar and wind availability, which could then be input into a large parameter model that could generate a result within our lifetime, so that multiple options could be considered and evaluated.

On the computational side, it is very important to be developing these advanced algorithms because the energy system problems that we are tackling are enormous. The good news is that these very large parameter models can be put together in order to look at the optimizations across that system, and can lead us to new insights in how to design and configure the future energy system. This is also a good example in use of external collaboration.

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Whether it is harnessing air, water, or solar energy, renewable power sources have become a forefront in energy advances. What are some benefits and drawbacks of such energy technologies?

The intermittency of the renewables has to be addressed as people's needs are 24/7 in terms of energy demands. Consider day / night and seasonal variations in solar and wind availability, as well as in heating and power. Renewable solutions have to be able to provide energy when it is needed, and not just when it is easy or convenient to do. The good news is that renewable options are cleaner and more widely available, but they are not available all the time, or at the same intensity everywhere in the world.

Land use around major cities -- where most people now live -- is an issue. Land is often expensive and has limited availability. We really have to look at developing energy carriers to move energy from resource-rich regions where land is available and cheap, to urban centers. There are great challenges and opportunities in providing vectors such as hydrogen for moving and storing renewable and clean energy in this manner.

You have worked on some specific case studies in New York City and Texas regarding synthetic fuels and chemicals production. Could you tell us a little more about these case studies?

We looked at moving renewable energy in the form of wind and solar from Texas to New York City in order to provide a portion of the electric grid supply. There is a penalty for making a carrier like hydrogen to do that - ammonia would be another example of a hydrogen-based carrier - but once the carrier has been made, you can take advantage of a higher resource intensity for solar and wind in Texas, which also has lower land-use costs, and then have the opportunity to move it over long distances to an urban location like New York. In doing so, storage capacity is also provided, as the carrier can be stored more easily in large quantities, than is the case for electrons.

Modeling shows a potential advantage in lower land costs, higher solar and wind intensity, and storage benefits, in spite of the fact that some energy is consumed in making the carrier and then converting it back to electricity. Those case studies were

a good example of moving renewable energy around, storing it, and getting it to the urban demand centers that are requiring it.

Taking into account the case studies that you have told us about your research from over the years and your time at Shell, what surprising obstacles have you faced during your research on energy and chemicals?

The major obstacle is the ability to predict the future. I have been amazed at how dynamic the energy and environmental sustainability situation has been over my career, moving from a complete lack of energy to an abundance, as a result of new technologies like the fracking and shale gas revolution, deep water production of oil and gas and the precipitous drop in solar PV and wind costs for making renewable energy.

Consumers also change their product preferences, relative weightings of environmental and economic stressors over time, which contributes along with external events to an ever-evolving energy landscape that requires an adept research community to respond to the changes in stakeholder interests and needs.

Keeping ahead of those changes is certainly the big challenge, this last year of COVID being a good example of a change in terms of how we are going about our business and work, our personal lives, what we are prioritize, and hence what we need to do to go forward. Expecting and being responsive to change, is key.

With COVID, how did you change? How did you adapt to that?

Our scientific and technical experts are distributed across the globe, for Shell across three major global hubs, so we accelerated the use of virtual meetings and tools to enhance collaboration, while reducing the need for travel. Cloud-based collaboration tools also allow spanning of different time zones for effective use of staff time.

It is possible to do remote monitoring of experimental programs using process control and database toolkits, so it is not necessary to be in the lab to get a good hands-on feel of what is happening. Virtual meetings and collaboration tools can be globally inclusive of all collective expertise, and one can fit in more meetings and

time for problem solving by avoiding the time spent on travel. I am sure we have reduced our CO_2 footprint from air travel by using the new tools, and that is going to continue into the future as a new best practice.

Air travel is one of the most significant sources of carbon emissions. What do you think the roadmap is for the introduction of sustainable aviation fuels?

Aviation is one of the great challenge areas because of the energy density required for effective design and operation of a jumbo jet, for example. The road transport sector is a large consumer of energy, and there are solutions in place such as battery electric and hydrogen fuel cell vehicles, but air travel especially in the larger jets is particularly difficult to decarbonize.

Batteries may work for very small planes on local routes in aviation, while hydrogen fuel cells may work for slightly larger planes, but for the largest intercontinental jet travel, a higher energy density fuel is needed. Hydrogen may not suffice.

For that reason, Shell is working on providing future clean fuels to tackle the problem of decarbonizing aviation. Biofuels can be used for this purpose, but Shell is also looking at direct air capture of CO_2, which can be reformed with renewable or clean hydrogen to make solar or zero-carbon fuels. These would be drop-in replacements for the jet fuels that are used today, but with greatly reduced footprints.

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As a current chair on the U.S. Department of Energy Hydrogen and Fuel Cell Technical Advisory Committee (HTAC), you are able to contribute scientific knowledge into policy. How has this experience shaped your work?

HTAC championed DOE partnering with the American Institute of Chemical Engineers (AIChE) for creation of the Center for Hydrogen Safety (CHS). This paved the way for a global institute for sharing best practices and safe handling of hydrogen, which is very important given the extent of new participants entering into the hydrogen arena.

In HTAC, industry, national labs and academic committee members can learn from each other in areas that include R&D and commercial developments for new fuel cells, electrolyzers for hydrogen manufacture, storage materials, hydrogen transport and dispensing, safety, as well as what is happening in the marketplace in terms of new mobility solutions and the availability of fuel cell vehicles and refueling stations.

That interaction helps us collectively to recommend and target what types of R&D should be done, how to leverage collaboration, and to encourage partnerships across the supply chain.

What advantages are there from using hydrogen as an energy vector and storage for renewables over more mature technologies like battery storage?

Both have their places in usage. A battery is 70 to 90% efficient in terms of storage but the problem is the energy density, the duration and the cost.

While it is a great solution for short term storage where relatively low-density systems are plausible, like your laptop or cell phone, hydrogen is better suited when higher energy density is needed, such as in seasonal storage of wind and solar or when energy is moved across long distances. They both have their opportunity space.

Shell is working on both, but each has its place to play as an optimum. Heavy-duty trucking, for example, requires the higher energy density that comes with hydrogen in order to make that a good value proposition relative to range and payload. Because hydrogen has to be made out of renewable or clean energy, a penalty is paid in terms of the roundtrip efficiency of making hydrogen as a carrier and then converting it back to electricity. The roundtrip or cycle efficiency is therefore less than for batteries, but storage and energy density are increased, which is important for longer term grid or heavier duty transit applications.

You are also a chief scientist in chemical engineering for Shell. What has been Shell's role as a company in the chemical engineering and fuel industries?

Shell has a very long tradition in leading innovations in energy. I am standing on the shoulders of some very excellent and famous engineers, scientists, and inventors that have been part of the company over its history of more than 100 years. It has been a great honor for me to help carry on this tradition.

Shell's staff have spanned a breadth of contributions from fundamental science and engineering in oil and gas production, chemicals production, expanding now to biosciences including biofuels and bio-based chemicals, and also things like

advanced process control and environmental catalysis which makes the industry cleaner and more efficient. Chemical engineering has been central to everything Shell has been doing on the surface in its facilities, as well as now the subsurface including opportunities in enhanced oil recovery, and capture and sequestration of carbon dioxide or CO_2.

One of Shell's flagship projects is the gas-to-liquids plant in Qatar, which is the world's largest. The plant converts natural gas into clean-burning diesel, and hydrocarbons that are intrinsically safe to humans and the environment for use as solvents or lubricants. This is an example of a major technology development that occurred in recent years using fundamentals of chemical engineering and catalysis across a multiple-step process, to implement advantaged cleaner solutions.

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Could you tell us a little bit more about what the future will hold for you in your research on energy and chemicals?

Shell is very excited about energy vectors like hydrogen for use as a clean, zero-

emission fuel across a wide spectrum of applications. Also, in prospects for future capture of CO_2 out of the air to make solar fuels or hydrocarbons that are renewable-based and hence can be burned without a carbon footprint penalty. That requires chemical engineering conversion, but we are working on all of the above to be able to provide a clean and environmentally advantaged jet fuel of the future. Biology can be used to help produce fuels and provide nature-based solutions for carbon mitigation, while advanced carbon capture and storage can provide opportunities for net negative emissions, or removal of CO_2 from the atmosphere.

Shell is also continuing to work on advanced biofuels, chemicals, and the circular products economy, providing an incentive to recycle plastics waste and prevent its loss to the environment.

Do you expect more technologies that will help us reduce plastic waste?

Indeed, there are some great technologies that combine renewable energies with plastics waste recycling, including use of electrification and hydrogen to provide the process heat. Those new trends couple the renewable or clean energy drivers with circularity to protect climate and ecosystems. Enabling efficient recycle will provide incentives for preventing the leakage of plastics into the environment.

What other renewable energy source applications will you be discussing at Pittcon this year?

I will be discussing clean sources of energy and how we integrate wind and solar, which has been our focus, into the energy system, as well as how we continue to use natural gas and bioresources, coupling those with CO_2 capture and sequestration to make them clean.

My talk will focus on managing the energy transition to achieve less than 1.5 degrees C temperature rise, while also providing for the energy needs of the developing world and for delivering on circularity for chemical products. I will paint a picture as to why so many new and different technologies are needed across this space, and dive into some of the laboratory and research opportunities that must be pursued to make this more efficient, given the enormous amount of new technology development that must be undertaken to make this happen.

When it comes to Pittcon, we are really looking forward to making connections with

providers of advanced methods and laboratory capabilities, and learning from others. Continuous improvement of our toolkits and capabilities is very important to achieve these ambitious goals.

How does Pittcon influence the realms of chemical engineering and energy science?

Pittcon is a great opportunity and space to learn about what is new out there in in the field, as well as an opportunity to network and communicate our challenges and needs so that new laboratory components and capabilities can be developed.

In the future, I see a much larger use of robotics in terms of how laboratory programs will be run. One can imagine doing a number of things that we do at the bench today using a robotic system where one can simply dial up or program a configuration needed for the moment, and then implement. This can increase speed and safety. Also, there will be more cross-learning in discovery chemistry via use of data analytics, augmented by machine learning and computational modeling to speed materials discovery.

I think Pittcon is a good two-way communication between what industries and research labs need, and the people who are providing solutions.

Are you looking forward to virtual Pittcon? What new trends do you think it will bring?

Virtual Pittcon is exciting. I personally have found that I can attend many more meetings, conferences, and workshops if not spending so much time on travel. With some creativity and effort, it is possible to get good at making new connections virtually, and visual tools including virtual reality are becoming more commonplace. I have seen some very interesting breakout and networking sessions using virtual tools, and am quite committed to making this work into a future beyond Covid, given the carbon footprint reduction it also offers.

For the attendees and audience, virtual presentations and recordings avoid time conflicts, and can be worked into one's schedule, so the potential is there to expand and see even more than could happen in person.

2020 has been a very different year. Why are events like Pittcon important for the science community to come together, now more than ever?

Our challenges are greater than ever and we need to be aware of new developments. I find networking to be tremendously valuable to keep in touch with, not only what our opportunities are, but also what are our stakeholders' interests are.

The act of presenting a conference paper certainly helps drive the research community forward to show latest results, and get input from peers on new developments. Peer input and feedback is a critical aspect of technology development and improvement, and in moving forward as a community by leveraging experience and knowledge. The learning opportunities translate back into what we are doing in our day jobs. I hope that the virtual aspect will be an advantage and we can do more of it in the future.

About Pittcon

Pittcon® is a registered trademark of The Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, a Pennsylvania non-profit organization. Co-sponsored by the Spectroscopy Society of Pittsburgh and the Society for Analytical Chemists of Pittsburgh, Pittcon is the premier annual conference and exposition on laboratory science.

Proceeds from Pittcon fund science education and outreach at all levels, kindergarten through adult. Pittcon donates more than a million dollars a year to provide financial and administrative support for various science outreach activities including science equipment grants, research grants, scholarships and internships for students, awards to teachers and professors, and grants to public science centers, libraries and museums.

What Pittcon Can do for You from AZoNetwork on Vimeo.

About Joe Powell

Joe Powell (Joseph B. Powell, PhD) is Fellow and former Director of the American Institute of Chemical Engineers, and served as Shell's first Chief Scientist – Chemical Engineering from 2006 until retiring at the end of 2020, culminating a 36-year industry career where he led R&D programs in new chemical processes, biofuels, enhanced oil recovery, and advised on R&D for energy transition to a net-zero carbon economy. Dr. Powell is co-inventor on more than 125 patent applications (60 granted), has received AIChE / ACS / R&D Magazine awards for Innovation, Service, and Practice, and is co-author of Sustainable Development in the Process Industries: Cases and Impact (2010). He chaired the U.S. Department of Energy Hydrogen and Fuel Cell Technical Advisory Committee (HTAC), and was elected to the U. S. National Academy of Engineering (2021) after serving two terms on the Board on Chemical Sciences and Technology. He served as guest editor of *Catalysis Today* Natural Gas Utilization, on the editorial board for Annual Review of Chemical and Biological Engineering, and was Crosscutting Technologies team lead and author for Mission Innovation Carbon Capture Utilization and Storage (2017). He currently advises in energy and chemicals and process development (ChemePD LLC). Joe obtained a PhD from U. Wisconsin-Madison in 1984, following a BS from U. Virginia (1978), both in chemical engineering.

Sensing a Healthier Future with Sustainable Nanomaterials and Biosensors

In this interview conducted at Pittcon 2024 in San Diego, we spoke with Professor Omowunmi (Wunmi) Sadik, this year's Keynote Speaker, about the transformative impact of sustainable nanomaterials on human health.

Could you please introduce yourself and your current position?

My name is Omowunmi Sadik. I am the department chair and Distinguished Professor of Chemistry and Environmental Science at the New Jersey Institute of Technology (NJIT). Additionally, I am the center director for the BioSMART Center, situated on the downtown Newark campus.

Could you share with us your journey in the field of chemistry and your current role at the BioSMART Center & New Jersey Institute of Technology?

I was born and raised in Lagos, Nigeria, in a family that strongly encouraged my pursuit of science. After completing my bachelor's and master's degrees at the University of Lagos, I pursued my Ph.D. in chemistry at the University of Wollongong in New South Wales, Australia.

Following my doctoral studies, I joined the US Environmental Protection Agency (EPA) for a National Research Council postdoctoral research position in immunochemistry. Subsequently, I began my independent career at the State University of New York at Binghamton, where I progressed from assistant to associate and finally full professor over a span of 24 years. Approximately five years ago, I transitioned to NJIT.

Your keynote presentation at Pittcon 2024 revolves around sustainable nanomaterials. What is meant by the term “sustainable nanomaterials,” and what initially sparked your interest in this area of research?

Sustainable nanomaterials are derived with a low carbon footprint. The design involves reducing the use of volatile organic materials and considering bio-renewable materials with 100 % renewability and biodegradability.

My interest in this field was initially sparked by the prevalent negative connotations associated with chemistry, such as toxicity and the use of volatile organics. We’ve witnessed concerns regarding substances like lead, mercury, and PCBs (polychlorinated biphenyls).

However, chemistry has contributed immensely to society. It has facilitated advancements in pharmaceuticals, improved health, and played a crucial role in enhancing food production through pesticides and herbicides. Additionally, chemistry has been central to energy production.

It is, therefore, imperative that we think about the potential role that chemistry can play in terms of sustainability. When we discuss sustainability, we must consider society, the environment, and the economy—the three pillars of sustainability. Sustainability is akin to a three-legged stool, with people, the planet, and profit at its core. Therefore, sustainability is crucial for our progress moving forward.

How was it to be this year's keynote speaker, and how did you find the talk yesterday?

Having attended Pittcon for the past three decades, I've had the privilege of participating in numerous Coulter keynote lectures. It's truly an honor to be named the 2024 Walter Coulter lecturer. I feel both delighted and humbled to be associated with those who have walked this path before me.

In your talk, you mention the use of sustainable nanomaterials to understand reaction mechanisms. Could you elaborate on how these materials aid in this understanding?

Understanding reaction mechanisms is crucial for addressing the unintended consequences of chemistry. While detection is important, comprehending the fate, transport, and transformation of chemicals in the environment and human health is equally important. Without this understanding, we only grasp part of the story. Therefore, I believe that delving into mechanisms is critical, and utilizing sustainable materials to understand these mechanisms is pivotal for comprehending their effects on human health.

Your work has significant implications in biosensing, especially for pain biomarkers and persistent pollutants. How do you foresee these applications evolving in the near future?

Pain biosensors are becoming increasingly necessary for objectively measuring pain. Pain assessment in healthcare settings often relies on subjective methods, such as asking patients to rate their pain on a scale of one to five. However, pain is highly individualistic, and this subjective approach can lead to inaccuracies. The International Association for the Study of Pain defines pain based on what the individual reports, emphasizing the subjective nature of pain perception.

Continuing to rely solely on subjective pain assessment methods may contribute to the exacerbation of the opioid crisis. For instance, if a person expresses their pain intensity as “10 out of 10,” it is crucial to acknowledge and respect their subjective experience. Denying or questioning their reported pain level undermines their experience and can hinder effective pain management.

To address these challenges, objective measures of pain are needed. Similar to glucose monitors that objectively measure blood glucose levels, we should explore the identification of biomarkers for pain and the design of devices capable of objectively assessing pain levels. This is the driving force behind my work in pain biosensors.

What is actually meant by the term biosensor?

Biosensors are compact devices comprising a transduction element closely associated with a biological molecule. This biomolecule interacts with the analyte of interest, triggering a response that is amplified through electronic components to provide valuable information.

A prime example is the glucose monitor, which typically employs electrochemical transduction linked with the enzyme glucose oxidase. When glucose in the blood combines with glucose oxidase, two compounds are produced: gluconolactone and hydrogen peroxide. While gluconolactone is not electroactive, if we measure hydrogen peroxide, we can indirectly determine how much glucose is present in the blood. That is a very good example of a biosensor.

Image Credit: Andrey_Popov/Shutterstock.com

Biosensors are versatile and can be designed for various applications. For instance, alcohol biosensors are used by law enforcement to detect alcohol levels in individuals suspected of driving under the influence. We can design a biosensor for almost anything.

Your biosensor technology for pain assessment is quite innovative. What are the key factors that led to its development, and how does it work?

A close friend approached me regarding their daughter's constant struggles with sickle cell disease. Doctors often faced challenges in accurately gauging the level of her pain, so she asked if it was feasible to devise an objective method for pain measurement.

This resonated deeply with me, as I believed such a solution should already exist. I assured her that with the right transduction and molecular tools, we could develop a sensor for this purpose. Our subsequent literature search revealed the absence of such a solution, sparking the beginning of our journey in the development of pain biosensors.

The pain biosensor operates by targeting cyclooxygenase II (COX-II), an enzyme responsible for converting arachidonic acid into prostaglandins. Prostaglandins are inflammatory markers associated with pain. By measuring COX-II levels, the biosensor detects the presence of these markers. COX-II has been extensively studied and implicated in various conditions such as inflammatory diseases, osteoarthritis, neurological disorders, and cancer.

Over the years, substrates have been developed to bind to COX-II, leading to the creation of medications like Advil, Vioxx, and Bextra, although these drugs have encountered issues. By understanding the biochemistry of pain and inflammatory markers like COX-II, we can design sensors tailored to detect them. This approach forms the basis of how pain biosensors function.

What challenges have you faced in researching and developing nanomaterials that are economically beneficial yet environmentally benign?

One of the primary challenges we face is persuading individuals of the significance of sustainability and the importance of designing sustainable materials. Over the past two decades, nanotechnology has been the subject of intensive study. During its early stages, two contrasting perspectives emerged: one suggested that nanomaterials are inherently toxic, while the other proposed their potential applications in fields such as biomedicine.

The first group focused extensively on investigating the environmental health and safety (EHS) implications of nanotechnology. Many organizations, including the National Nanotechnology Initiative (NNI), were proactive in addressing these concerns from the outset.

The NNI, which involved over 25 federal agencies, played a central role in coordinating efforts to understand the EHS issues associated with nanomaterials. Agencies such as the US Environmental Protection Agency (EPA) and the National Science Foundation (NSF) provided funding to support researchers in this field.

Another critical organization in addressing the sustainability of nanotechnology is the Sustainable Nanotechnology Organization (SNO). SNO, a 501(c)(3) organization, serves as a platform for professionals across various disciplines, including scientists, engineers, social scientists, and economists, to engage in discussions regarding the

advantages and disadvantages of nanotechnology.

For those unfamiliar with SNO, I encourage you to visit www.sosnano.org.

As the co-founder of SNO for the past 13 years, I have witnessed annual gatherings where practitioners convene to explore these topics. Thanks to proactive measures taken by individuals and organizations, such as those supported by the NNI and SNO, there has been a significant shift in the conversation surrounding nanotechnology. Rather than viewing nano as inherently toxic, there is now an emphasis on designing nanomaterials with safety and sustainability in mind.

Can you discuss the roles of electrosynthesis and sonochemistry in the development of safe nanomaterials?

Electrosynthesis allows us to create nanomaterials using electrons. It is a safe method that sidesteps the need for volatile organic substances. Sonochemistry operates on a similar principle, utilizing sound and acoustics to achieve material synthesis. These methods align with the ethos of green chemistry, alongside photochemistry and electrochemistry, as they prioritize sustainability and environmental responsibility in material production.

You are the Co-Founder of the Sustainable Nanotechnology Organization. Could you tell us more about the goals of the organization, as well as the work the organization does?

I had the honor of being the inaugural president and co-founder of SNO. My colleague, Barbara Kern of the EPA and also NSL, joined me in this endeavor. Our aim was to establish a platform for nano practitioners to convene and engage in constructive dialogue regarding the advancement of nanotechnology.

Today, under the leadership of our current president, Dr.Achintya Bezbaruah, SNO continues its mission to promote research, education, and responsible development within the field of nanotechnology.

It’s fascinating to see how the conversation has evolved. Now, the focus extends beyond discourse to tangible applications. For instance, if you’ve received the Moderna or Pfizer COVID vaccines, you’ve already been exposed to

nanotechnologies. This shift underscores the positive potential of nanotechnology and the importance of responsible development.

As we mark the 75th anniversary of Pittcon, could you share your first memory or experience of attending this conference and how it impacted your view of the scientific community?

My first Pittcon experience dates back to 1993, over 30 years ago, when I was a grad student traveling from Wollongong, Australia. Encouraged by my mentor and advisor, Professor Gordon Wallace, I found myself immersed in the excitement of the event.

I attended various technical sessions, and it was particularly beautiful to see that we were not alone in the work that we were doing in the lab; others were also delving into similar realms of chemistry.

The exhibition floor was just as exciting as I had the opportunity to see some of the companies and instrumentation that I had only ever encountered in literature – Dionex, Waters Corporation, and Shimatsu, among others, were all present.

Since then, I've made it a point to return to Pittcon time and time again. The allure lies in several factors. Firstly, the networking opportunities are unparalleled. Pittcon brings together the luminaries and influencers of analytical chemistry and applied spectroscopy, fostering connections and encounters with old friends and esteemed professors.

I vividly recall one instance at a SEAC dinner where I found myself seated across from Professor Allen Bard, whose electrochemistry textbook had been like a Bible to me. Though initially starstruck, a chance conversation during the break led to Professor Bard warmly introducing me to fellow attendees, catalyzing my integration into the community.

Additionally, Pittcon offers invaluable short courses covering many topics. The exhibition floor, with its array of cutting-edge instrumentation and technologies, never fails to captivate me. In essence, Pittcon is more than just a conference; it's a hub of learning, networking, and inspiration that keeps me returning year after year.

Finally, what are you most looking forward to at Pittcon 2024 in San Diego?

The weather in San Diego is always beautiful, so selecting a seaside location for the event is a fantastic choice. As you know, at this time of year, snow is on the ground on the East Coast, so this will be a welcome change to enjoy the pleasant weather there.

I'm especially looking forward to the technical sessions and sharing this experience with my students, two of whom will be presenting. As always, I'm excited about the networking opportunities that Pittcon always brings.

About Professor Omowunmi (Wunmi) Sadik

Dr. Sadik is a Distinguished Professor and Director of The BioSMART Center at the New Jersey Institutes of Technology (NJIT). She has held appointments at the State University of New York at Binghamton, Harvard University, Cornell University, the US Environmental Protection Agency, and the Naval Research Laboratory. Sadik holds five patents for her work on biosensors and nanostructured membranes and has published over 200 peer-reviewed works with 400 invited lectures and conference contributions. Her group focuses on understanding interfaces, particularly the electrochemical interface, and how to use the knowledge gained to pursue the development of innovative bio (analytical) sensor technologies that improve human health and the environment. Sadik has developed biological sensors for objective pain assessment, electrochemical sensors for heavy metals, proteins, and organic acids, and a portable, fully autonomous, and remotely operated sensing instrument known as the U-PAC (Ultra-Sensitive Portable Capillary Sensor). At BioSMART Center, she is leading the efforts to create sustainable nanocatalysts to detect and degrade recalcitrant pollutants such as PFAS, 1,4-Dioxane, and micronanoplastics. Sadik is a fellow of the American Chemical Society, the Royal Society of Chemistry, the American Institute of Medical and Biological Engineering, and the National Academy of Inventors. As the Co-Founder and Inaugural President of the Sustainable Nanotechnology Organization (www.susnano.org), Sadik is building support for Science and promoting the understanding of its broader relevance to society.

About Pittcon

Pittcon is the world's largest annual premier conference and exposition on laboratory science. Pittcon attracts more than 16,000 attendees from industry, academia and government from over 90 countries worldwide.

Their mission is to sponsor and sustain educational and charitable activities for the advancement and benefit of scientific endeavor.

Pittcon's target audience is not just "analytical chemists," but all laboratory scientists — anyone who identifies, quantifies, analyzes or tests the chemical or biological properties of compounds or molecules, or who manages these laboratory scientists.

Having grown beyond its roots in analytical chemistry and spectroscopy, Pittcon has evolved into an event that now also serves a diverse constituency encompassing life sciences, pharmaceutical discovery and QA, food safety, environmental, bioterrorism and cannabis/psychedelics.
