Who will be the next Face of Mass Spectrometry? Nominate a member who exemplifies diversity of ASMS (nationality, ethnicity, age, etc.) and path to a career in mass spectrometry.

FACES OF MASS SPECTROMETRY / Athula Attygalle

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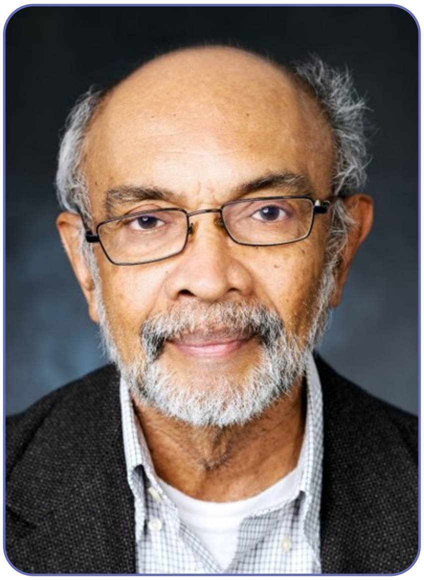

A Global Venture

Athula Attygalle's life and work embody the value of multiculturalism in the field of mass spectrometry. During his initial scientific education in Sri Lanka, nearly 40 years ago, he had neither heard of nor been able to access mass spec instrumentation. Later, after moving to Japan, he was first introduced to the instruments of mass spec, but he was not yet able to access any to do his own independent work. Eventually, while pursuing further education and opportunities in England and Germany, he began working with techniques and instruments of mass spec in his own research.

Athula relocated yet again in 1989—this time to the United States. Soon after, he became the Director of the mass spectrometry facility at Cornell University. During this period, he began to focus on analytical chemistry while working with unique analytes such as defensive chemicals released by beetles. A paramount research endeavor from his career is his invention of a helium-plasma ionization method (HePI) that consumes helium very economically. Numerous applications for HePI have since been developed, to detect analytes as diverse as involatile inorganic salts, explosive residues, pharmaceuticals and heavy metals.

Athula credits the multicultural nature of his career for helping him be a better mentor to students from different nations and for facilitating collaborations with researchers from all over the world. He believes the scope and future of mass spectrometry is dynamic and will continue to evolve in the next few decades. Possibilities for global collaboration in the field will help its expansion, and scientists like Athula exemplify the innovative research that mass spec can produce when it draws upon creative ideas from many nations and cultures.

How did you get your start in mass spec? Was it growing up in Sri Lanka? Or, was it after you came to the United States?

Actually, it was neither. In Sri Lanka, I did my first degree and my master's degree, and I was studying basics and fundamentals of chemistry. We had no mass spectrometers, and I'd actually never even heard of one. After I got my master's in biochemistry, I went to Japan on a UNESCO scholarship, where I saw these wonderful mass spec instruments, but I was not allowed to touch them. Then, while conducting my Ph.D. research in England at Keele University, my mentor Prof. David Morgan was interested in how ants communicate with each other using chemical signals. These chemicals ants use, particularly to lay trails, are called pheromones. The challenge was how to identify and characterize these chemicals that ants produce in ultra-minute quantities. Each ant stores only a few nanograms (millionths of milligrams) of these chemicals. The only technique that was sensitive enough to study and characterize such chemicals was mass spectrometry. That was 40 years ago, so there were no computers controlling the instruments.

The magnetic-sector instrument I used was a monster that occupied half the room. Spectra were not acquired and stored, but they were recorded in real time on chart paper or on light-sensitive photographic paper. Once recorded, peak heights were measured manually with a ruler. Also, the spectral peaks had to be measured immediately (and that created many sleepless nights), because the peaks would disappear after a day or two. The instruments were controlled with a bunch of adjustable dials. Cleaning and taking care of instruments was a nightmare because there was no YouTube or online instructions—not even a printed manual! Taking a source apart was easy, but putting it back together was a challenge. There were 100 different ways of putting it back together, most of which were wrong. But those circumstances allowed us to master the instrument and work with a clear mind, as though we were doing magic, in the untrained eye of the bystander. The first lesson to be learned was how important it is to become the master of the instrument and not its slave.

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Athula Attygalle, Valisha Edwards and Sihang Xu working with the SYNAPT-G2-HDMS Q-ToF Mass spectrometer. (Photo courtesy of Athula Attygalle.)

How and when did you decide that you were going to specifically focus on analytical ?

Characterizing biologically active molecules available only in ultra-minute quantities as complex mixtures was a fascinating challenge. That is why I wanted to become an analytical chemist. While I was working in Germany, I met a professor from Cornell at a meeting. We had some discussions, and then he asked me to come to Cornell as a visiting professor, which I ended up doing after discussing it with my family. Originally, I was only going to stay there for a year, but that year became 12 years! At Cornell, I developed on analytical chemistry, and I taught a course in it. Cornell not only had good instruments but also had mass spectrometry giants like Professor Fred McLafferty, who is best known for the McLafferty rearrangement reaction in ion fragmentation. Soon, I became the director of the mass spectrometry facility at Cornell University, an amazing place. We had good training on looking after the instruments, taking them apart, and putting them back together. It provided me the opportunity to work with a very wide range of analytes, and to look at all sorts of samples—it gave me a very good background to work with both small and large molecules.

What brought you to your current position at Stevens Institute of Technology?

While I was at Cornell, I met the Dean of the Science Faculty at Stevens at that time, along with a trustee who was a big entrepreneur. They were interested in my work, and they asked me what it would take to make me join Stevens. I said, "I work with expensive toys—give me a state-of-the-art instrument!" This they did, and so, I moved to Stevens in 2001. It has been a great opportunity to start and lead my own independent research team.

What findings have you discovered in your work with beetles?

Beetles are a fascinating group of insects (and specifically, the bombardier beetles have a very fascinating chemical defensive system). If you take all of the species living on earth, beetles are the most dominating. With over 400,000 described species, they are the largest of all orders, constituting almost 40% of described insects, and 25% of all known animal life forms on earth. What is their secret of success? Chemistry. Chemical weapons.

At Cornell I worked with Professors Thomas Eisner and Jerrold Meinwald, both pioneers in chemical ecology, who studied chemical weapons of arthropods. It was a very enjoyable and productive collaboration. Using mass spectrometry, I could identify hundreds of chemicals used by insects—spiders and millipedes, for example—for their defense. At Cornell, I also met Kipling Will, who was working on the systematics of beetles. Later, he became a professor at the University of California, Berkeley. We were both interested in the chemical defense mechanism of the bombardier beetle. When challenged, these beetles make an obnoxious chemical mixture on demand and spray it at the enemy. Not only is this obnoxious chemical mixture made on demand, but it is also heated to 100 degrees centigrade (the boiling point of water) just before it is sprayed at the enemy. The chemistry was already known, but it was not clear how these beetles could mount such an effective defense with chemicals synthesized on demand, and within such short time.

Mass spectrometry was sensitive enough to provide a way to work with one beetle at a time. We made a hypothesis, and to test it we made stable isotope-labeled chemical precursors, which we sent to Berkeley. Kip would feed them to beetles, collect the secretions, and send the samples to Stevens. Using

Some members of the current Attygalle research team, from left: Ali Virani, Idris Junaid, Jinxin Zhang, Athula Attygalle, Ishira Samarasinghe, Shimin He, Kinan Khanzada, and Sihang Xu. (Photo courtesy of Athula Attygalle.)

mass spectrometry, we were able to follow the biosynthetic pathway and decipher the secrets of the chemical weaponry of the bombardier beetle. We have also demonstrated how to use gold nanoparticles to detect HCN by laser-ionization mass spectrometry. Millipedes (even almonds, cherry pits and apple seeds) produce HCN precursors for their defense. Nano quantities of HCN (a very toxic chemical) present in the atmosphere can also be monitored and detected by this technique. So, this work with beetles and millipedes has provided many findings that have been both interesting and useful.

Which countries have you worked and trained in? How has meeting people of different cultures in those countries influenced your work?

Being multicultural helps to gain the trust of people who come as students from different corners of the earth, and it facilitates collaborations with many researchers all over the world. My immediate family consists of four members, and all four were born in different countries. I get invitations to conduct teaching workshops in many countries. For the last 20 years, I've gone to the Max Planck Institute in Germany every other year to train people on mass spectrometry. We have also had good collaborations with groups in Malaysia, Pakistan, India, Saudi Arabia, Germany, Brazil, and the Dominican Republic. Here in the United States, I always have many international students and collaborators who have worked and contributed to discoveries made at the Center for Mass Spectrometry at Stevens.

Tell us about the 2014 Inventor of the Year Award given to you by the New Jersey Investors Hall of Fame.

This was primarily for our invention of the helium-plasma ionization method (HePI). Plasma ionization was previously known, but our invention consumes far less helium than any other existing method. Helium is an endangered element—whatever amount we have now, when we finish it, it's gone. If and when that happens, there will be, for example, no cryogenic methods to develop what we call super-cold magnets, nor will there be any MRIs. So, we must economize helium as much as we can. The microplasma we generate in HePI requires only a few milliliters of helium per minute—I would call it a very green technique. We have some patents on it, and I hope we will have a commercial instrument soon. It's a major improvement in how to ionize molecules at atmospheric pressure, using very, very small quantities of helium—and it's a very versatile technique.

What kinds of academic mass spec facilities have you run? Has being a mentor to students as a professor influenced your work at those facilities?

At Stevens we train students on many different instrument platforms from different vendors. We are fortunate to have a variety of ionization techniques and different mass analyzers. Students can learn hands-on how to use different software systems from different vendors, which increases their laboratory skills. So, they have no problem in gaining employment. Some students work in industry part-time—they come in during the evenings and to get hands-on experience on different instruments. This way, they can develop their careers. The employment opportunities in mass spec are huge, and we can supply skills to that demand. The more versatile training we give them on many instruments and software platforms, the more assuredly they can go out there and fit into any laboratory.

What are your interests outside of the lab? Do they include travel?

Naturally, I receive invitations that involve a lot of travel. Another one of my interests is collecting books by philosophical authors such as Isaac Asimov (I have a huge collection of his books), Richard Feynman, and Arthur C. Clarke, among others. Isaac

Asimov wrote about 500 books in his lifetime. I don't know how he did it, especially considering he only had access to a typewriter at that time. It's difficult for me to even read that many books! But it's fascinating—he wrote books on many subjects, from Shakespeare to biochemistry and physics to science fiction stories and novels. These books give me stories to tell students about how to think differently and how to avoid dogmas or whatever gaga we hear all the time today.

This concept is very relevant to mass spectrometry in particular. That's because when we interpret a spectrum, we often start with a lead structure or a precursor structure, and we may draw some arrow pushes based on our classical learning on the paper right away, thinking it is the correct structure. But with our modern techniques, we are beginning to understand this is frequently incorrect—often, you can't represent a chemical by one single structure, because it may have different forms (tautomers, for example). I think of these as multiple personalities—a Dr. Jekyll and Mr. Hyde kind of situation. With the introduction of ion-mobility into mass spectrometry, we now have a new tool to monitor the fast transformations that occur between different tautomeric ionic structures in the gas phase.

> *"I think mass spectrometry has a lot of scope for the future—it's still an unfinished business."*

How do you envision the future of mass spec?

I think mass spectrometry has a lot of scope for the future—it's still an unfinished business. There are still loads of challenges, especially about generating gaseous ions and determining their structures. So, we can expect many new and dynamic developments. Every year, it keeps on evolving. Unlike some of the other sciences, the mass spec has recently grown out of proportion. If you go to the meetings, you see how the membership has increased—as I said, it's a very, very dynamic field. I think it has the potential to be one of the leading analytical fields as we enter the next decades!