Joseph Loo

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The Accidental Spectrometrist

Joe Loo is an adept storyteller. Fresh from a proteomics conference and an NIH review panel, he has carved out time for a conversation before catching a plane home to the west coast. But after 50 minutes, he has only mentioned specific details about his current research when pressed. Instead, he paints his journey as an analytical chemist with broad, easily followed brush strokes—and self-deprecating asides.

Loo has been a professor of biochemistry at the University of California, Los Angeles (UCLA) and Faculty Director of the UCLA Mass Spectrometry Instrumentation Center since 2001. More recently, he became the Editor-in-Chief of the Journal of the American Society for Mass Spectrometry which fields around 400 manuscripts a year. As he casually mentioned, "This morning, before you called, I was working on a number of papers. Every day, there is something for me to do for the journal."

After receiving his doctorate in analytical chemistry from Cornell University in 1988, he moved to a post doc position at Pacific Northwest National Laboratory (PNNL) where he began working on developing new mass spectrometry (MS) methods to characterize peptides and proteins for biomedical research. Over the next three decades, he has published well over 300 peer-reviewed and invited articles and book chapters, and he sports an exceptional h-index of 70 (Web of Science).

Even so, when asked to characterize his path to mass spectrometry, Loo characterizes his career as "an accident, really."

What is your professional background?

My background is a little bit unusual in the sense that I worked in industry for nearly 10 years for a "small" company named Parke-Davis (and later acquired by larger Pfizer Pharmaceutical). We did classical pharmaceutical research using mass spectrometry on small molecule drugs and the proteins that they target, and, at the same time, we started a proteomics group. This was in the 90s when proteomics was just starting to come onboard.

I would have stayed except that Pfizer came along with more of a business mindset, cutting projects if they had not reached important milestones. I understand the reasoning, but, as a scientist, it is hard to put your mind in that frame that "you've made good progress, but that drug won't go to the market fast enough so we need you to work on something else." My wife—she was also working at Pfizer—and I decided to take a leap and moved into academics at the end of 2001. What could go wrong? At the time, I thought "what the heck, if it doesn't work out I can always go back to industry."

How did you get started in mass spectrometry?

It was by luck. I grew up in the early 60s, way, way up north in New York State. My dentist was in Canada—it was easy to cross the border—and we were one of the very few Asian families in the town. My father was a professor of engineering at a small college where I went to study chemistry. At the time, I was enamored with TV shows that were pre-CSI like 'Quincy' that featured analytical lab work. When I got to graduate school at Cornell, I wasn't thinking about mass spectrometry, but Fred McLafferty was looking to apply MS to bioanalytical science research, and for some reason he took a risk on me. My project turned into a technique that no one uses today, for good reason. My project was to develop a novel radioactive source to ionize large biomolecules for detection by high resolution mass spectrometry [Loo, J.A., *et al., Anal. Chem.* **59**, 1880-1882 (1987)].

The post doc at PNNL got me on a path that really accelerated my own development. Dick Smith had just started to use this new technique called electrospray

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ionization. At that time, we were probably one of only three labs doing this around the world, and everything we did was brand new. It was smooth sailing. I'd go into the laboratory, make some measurements, and write a paper.

Did you have a favorite project?

We were the first group to demonstrate that you could take a large protein molecule, smash it to bits into smaller fragments – all in the mass spectrometer - and then use it for sequencing. Today, we call it top down mass spectrometry. Back then, we had clunky computers and equipment that looked like a science fiction movie from the 1950s. The mass spectra coming out on the screen looked like fragments were made, and then when you sat down and tried to work it out on paper, you see that you'd sequenced part of a protein. I couldn't believe it: all of the sudden we had a new technique [Loo, J.A., *et al., Science* **248**, 201-204 (1990)], and when I moved on to pharmaceutical research, I took this tool and methods for measuring protein complexes with me [Loo J.A., *Bioconj. Chem*, **6**, 644-665 (1995)].

What are you working on now?

I only have one trick. I am an analytical chemist, and that is what I will be forever. I am still trying to sequence proteins better than we could in the early 90s: faster, with more sensitivity, and apply it to biomedical research.

The focus in my lab right now ranges from developing biomarkers to address Alzheimer's and Parkinson's disease, traumatic brain injury and radiation exposure to understanding the role of post-translational modifications in biology. (And I still love to smash big proteins.) I have about 10 students and post docs and probably over 10 different projects. We work on fundamental science, but half my lab is applying our tools to medical or biochemical research. I am blessed to have great collaborators at my doorstep at UCLA, all working on cool projects. And my wife, Rachel Loo, also works in the laboratory. We have an interesting dynamic. I am not sure I would recommend the lifestyle; it is like a 24 hour group meeting every day. It's driving to work… group meeting; driving home… group meeting. We are always talking about science. Sometimes people get us confused because we publish so much together. It is the most boring lifestyle, if someone were to look at it externally (but of course, I would not change it for the world).

What else do you like outside of the lab?

When I was in industry, I had time to play tennis and golf. But when I got to academia, I found there is more work to be done, so I don't make time for hobbies other than watching sports and food shows on TV, reading email, and enjoying the benefits of traveling to scientific conferences. I have a younger cousin who lives in the LA area who gives me an excuse to see superhero movies. Tomorrow, when I get home, I need to see the movie *Venom* with him.

Do you have other challenges?

To try to always be original. In academics, you are always searching for the next development to stretch the field and to push yourself to stay in front of the pack. It's hard. As a field, mass spectrometry has grown so large, with more and more people coming up with great new ideas. A challenge is to get our students to think this way. It is great that they are learning how to do research, but how do you teach them to be creative and to always continue to learn and push themselves? That's not so easy. Students come from different backgrounds, and you have to dissect the motivation for each student and push the right buttons to help them grow best.