FACES OF MASS SPECTROMETRY / Barbara Larsen

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Taking a Seat at the Table

A true pioneer for women in the field of mass spectrometry, Barbara Larsen has built an impressive resume. She has made a profound impact on the ASMS in various leadership positions, ultimately ascending to ASMS president from 2006 to 2008. In that role, she was instrumental in helping two prominent female scientists gain international recognition as recipients of the prestigious Thomson Medal the first two women ever to earn that honor.

Barbara carries a sound knowledge base for a myriad of topics within the mass spectrometry field, from electrospray, thermospray, and magnetic sector instruments to newer instrumentation for analyzing enzyme products and probiotics. Yet regardless of what specific part of the mass spectrometry arena she might be delving into, she is always sure to apply the same principle to her work: "fitness for a purpose "or making sure the best tool possible is utilized to tackle the problem at hand.

Barbara had a distinguished career at DuPont in Delaware for many years and is now Senior Technical Fellow with IFF (International Flavors & Fragrances, Inc.), which recently merged with the DuPont Nutrition and Biosciences Business Division in which she now works. She bears a great passion for inspiring other female scientists who are eager to get their names f ront and center in the mass spectrometry field. Her message for them is simple: You cannot just sit back and let others in the room do the talking. It is all about having the courage and the initiative to actually take a seat at the table and to engage in the discussion.

How did you get your start in the mass spectrometry field?

In college at Santa Clara, I was introduced to the subject and it appealed to me. After college, I decided to go back to graduate school to learn more about mass spectrometry (MS). I ended up applying to University of Delaware, and after they accepted me, one of the professors there, Burnaby Munson, was working with gas chromatography–mass spectrometry. When I spoke to him, I felt like I needed to know more about electronics and tools than I did at the time. Then, I spoke to another professor, Doug Ridge, who was using an ion cyclotron resonance MS for his research and he made me feel at home in the laboratory. As a graduate student, I learned how to operate instruments, clean them, take them apart, and put them back together again. Doug and I went to the University of Nebraska to work on a triple sector instrument, and I realized that while I had a good fundamental understanding of instrumentation and operation, I needed more practical applications. I was able to do my postdoc with Catherine Fenselau at Johns Hopkins University. I learned fast atom bombardment and worked on interfacing thermospray to a magnetic sector instrument. I was hired by DuPont, where I was part of a centralized analytical department until 2017, when I transferred into what was known as Industrial Biosciences. Most recently, the business was spun off to merge with IFF in February 2021. In my current position, I am applying proteomics and protein characterization to enzyme products. The data generated helps us to understand our fermentation products and their protein composition. The data assists in identifying the post-translational modifications and what they mean to the enzyme functionality.

Tell us about your work on improving enzyme production and probiotic organisms.

For the probiotic effort, we were using all of the fermentation data that was being acquired and all of the "omics" data (metabolomics, proteomics, and genomics). By combining all the data, we developed an understanding of what was happening at different points of fermentation. Alternate fermentation conditions helped improve long-term stability of probiotics for the organisms we were working with. We could follow what pathways were being upregulated as we were making certain changes. From the proteomics data, we could see the surface layer proteins and could follow that the levels remained unchanged through evolution experiments we

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Barbara Larsen in the lab (center), with Sergio Nanita (left) and Sunny Li (right).

performed to improve shelf stability. We were using proteomics to understand whether we were making any changes in the organism, and we were finding that we had fairly stable compositions. With the enzymes, we are studying the enzyme composition and post-translational modifications. We are using the information to reduce the proteases that are excreted.

What is it about the American Society of Mass Spectrometry that has made you want to serve with them for such a long period of time?

It is a very tight community even as the society has grown over the years. The board genuinely cares about the science and started the journal to expand the dissemination of the science. And that was part of the reason why I was really enamored with the society, because of their approach to nurturing the science and making it more available to diverse groups of people. The board really works to pull younger people into the society by getting them involved in the society early. Another fantastic opportunity that I've been given is serving on the society journal's advisory board. One of the best parts is the people that you meet. It is all about developing relationships, expanding your knowledge, and making new friends. Also, serving on journals helps you understand what those journals need and how to improve your own papers.

Your passion centers around "fitness for purpose." What does that mean?

In an industrial setting, you usually have a diverse analytical laboratory with a variety of different tools. Depending on the problem that is being presented, you need to select the appropriate tool. For instance, do you really need a triple quad to quantitate something when you could use a colorimetric assay that would suffice to determine the amount of protein present? Could you use UV absorption? You do not need a mass spectrometer for that. There are times where you do need absolute precision, which would require a different kind of measurement. Or maybe you need to do more structural characterization, so you'd need to determine the elemental composition. Then you would use a high-resolution mass spectrometer. My "fitness for purpose" is being able to use the appropriate tool to make the right measurement for the problem at hand. For example, if you are going to be making a package for the EPA or the FDA, it is best to use a third-party laboratory for all the measurements. There's no question then on the limit of detection or the validity of the data. "In a corporate world, with limited resources and many problems to solve, you really need to choose the right tool to answer the questions."

What are your contributions to the development of electrospray ionization on a magnetic sector instrument?

That was one of the first projects I was given when I started in DuPont in 1984. DuPont purchased an electrospray ion source (ESI) from John Fenn. One of his graduate students came down and helped with the interface to the mass spectrometer. One of the difficulties was the weak pumping capacity of the magnetic sector instrument. So, I expanded the source design in order to get sufficient pumping. I generated a spectrum of water clusters, which was exciting because I finally got a spectrum. Unfortunately, that particular instrument was boxed up in preparation for room renovations. We had a new instrument installed and started working with John Fenn again, obtaining a newer ESI source. I had experience as a postdoc working on a thermospray interfaced to a magnetic sector instrument. What I learned there helped augment what we did with the magnetic sector instrument, which required floating the source mechanical pump at source voltages. Putting ESI on a magnetic sector instrument provided us something that nobody else had at the time, which was resolution. We had a high-resolution spectrum for cytochrome c and myoglobin, demonstrating isotopic resolution. We also started to see in-source

William and Barbara Larsen visiting a local in Australia.

fragmentation. Because we had resolution, we could see whether the fragments were singly, doubly, or triply charged. That helped with the manual interpretation of the fragmentation spectrum. The paper on this topic was probably one of my favorites that we published.

Tell us about your time as president of ASMS from 2006 until 2008.

In order to be elected to this particular position, you must have served on the board previously. I was the first person from industry to be to the position of president, and I received support from my management to perform this role. I met an inordinate number of people through this process and made a number of good friends. You end up meeting a variety of people who are outside your own background and experience. I have contacts that I still use today from that position. As a past president, you interface with the International Society for Mass Spectrometry, and one role is providing nominations for the Thomson Award. I was able to write two strong nominations for Catherine Fenselau and Catherine Costello. They were the first two women to be recognized for the award. That was something I'm most proud of having accomplished.

How did serving as president help you to grow as a scientist and a mass spectrometrist?

I learned how to have difficult conversations. In that position, you need to be the face of the society. I tend to be kind of a reserved, quiet individual, but I learned that I could convey the message for the society. I just kept my message clear and succinct. That assisted me within the DuPont corporation by helping me have the confidence to convey the results of science or changes that were affecting the group. I learned to communicate with impact. Also, by attending the conferences, I was always obtaining new scientific leads. I always seemed to get a little bit of advance notice on instrument developments and knew what to watch for in future purchases.

What are your interests outside the lab?

I'm an avid tennis player, so I like to play tennis with my friends. We have a USTA team, and I'm also very cognizant of what's happening in the professional world of tennis. I had a phenomenal trip last year when we went to see the Australian Open. I am also learning to play golf because I'm married to a very enthusiastic golfer. I'm in the beginning stages of learning, but I'm having fun. I've also become interested in sewing. And I'm always looking for a good novel to read or an interesting place to visit on our next trip.

Do you have a message for female scientists who plan to enter the industry sector?

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While mentoring, one of the recommendations for scientists working in industry is to maintain your skill sets. Look to maintain an external presence in your science. With mass spectrometry, we have the luxury of having local discussion group meetings which are held in the evenings during your personal time. These personal interactions you develop are so important to you as a scientist. If you are looking to maintain a presence like I had, you have to be publishing, presenting, and volunteering for some of these external organizations. So, those are my recommendations if you want to maintain a science-oriented industrial career. There are those who want to go into the management side, which I avoided, but it is encouraged because women in high-ranking positions within companies help with diversity. One of the things I once read, and that I try to live by, is to make sure you "take a seat at the table," both literally and figuratively speaking. When you are invited to a meeting, you cannot just sit in the back row. You actually have to sit at the table, because women tend to let others go first. You need to be part of the conversation.