

FACES OF MASS SPECTROMETRY

Brian Searle



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Mass Spectrometry Meets the Business World

Brian Searle loves the work that he does, but he admits that he would also have enjoyed becoming a professional potter, spending his days in a studio in the woods. With a mindset to pursue innovative change, he has always been optimistic about life's possibilities.

Diverging from a straight career trajectory during his pursuit to turn ideas into reality has taken Brian on an exciting career path. It was not long after he had earned his undergraduate degree and started working in a proteomics lab that he first started acting on entrepreneurial impulses that would ultimately lead to great successes.

Brian became fully committed to growing a thriving software business that now provides leading-edge software solutions to the mass spectrometry analytics community. While he has always been interested in science and finding solutions, he is also people-centered and values being part of a network of scientists. After 10 years in business, it became the right time for Brian to continue with the company while also returning to graduate school to continue his studies. This time he had a treasure trove of experience, including (but not limited to) his original focus on organic chemistry.

Once he had decided that he wanted to teach, networking with ASMS members helped Brian to find his fit at Ohio State University. He has now officially launched his academic career and is an assistant professor at the Ohio State University Medical Center in the Department of Biomedical Informatics.

A two-pronged career suits Brian well, as he will not only have opportunities to take on projects that present new challenges, but he will also be able to inspire others.

The fascinating combination of bioinformatics, proteomics, and mass spectrometry that is part of Brian's work has already inspired other computer programmers to become involved in the mass spectrometry community. Brian says that mentorship has been an important part of his career and he looks forward to mentoring an expanded group of students.

As an active member of ASMS, who even served on the ASMS Board while in grad school, Brian has a great deal of positive commentary to provide about his involvement. The community that Brian found at ASMS has had a significant influence on his career. He commented that "having access to this great network of interesting people has been what has made my career both fun and successful."

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

I started out doing organic chemistry as an undergrad student but ended up trying to find a career that wasn't organic chemistry, because I actually didn't think I was that great at it. One skill I did have was being able to write software, and that landed me into a bioinformatics job in a fledgling proteomics lab at OHSU in Portland, Oregon. After a few years I had been planning to go to grad school—I had accepted a slot at a university and was very much on that trajectory. Around that time Mark Turner, a colleague of mine, and I went to a small invite-only conference at NIST. During this meeting, Mark and I were sitting up late, and we decided that we wanted to start a company with Ashley McCormack, who was my earliest mentor in proteomics.

I withdrew from the university, and we would sit around Ashley's dining room table and sketch out ideas for our new company, Proteome Software. Ironically, we were unable to get intellectual property access to the software that we had planned to release from OHSU, so we ended up picking our next best idea, which was a new program idea called "Scaffold". We were lucky: it became a success and now it's used in thousands of labs across the world. A collaborator of mine once said that he tried to reinvent his research work every decade to stay fresh, and at the 10-year point, I decided I also needed a change. I had always wanted to be an academic, so I quit my day job and finally went to grad school at the University of Washington under Mike MacCoss. Afterwards, I did an independent postdoc at the Institute for Systems Biology and now I'm at Ohio State University living the academic dream.



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Brian setting up an Orbitrap tandem mass spectrometer for an experiment. Photo credit: Julia Haskin

What are some of the challenges and rewards of running your business?

The company has been an overall success, and that has been great. To me, an underappreciated aspect was that it was also an avenue for me to skip some steps and be a part of the academic mass spectrometry community without having the typically required credentials to be part of that community. I was able to give talks, teach, and live the academic dream without actually being an accredited academic. But the thing that has been most important to me is that it really gave me the steppingstone to be the scientist that I wanted to be and to guide the trajectory of what I wanted to do. It gave me a lot more freedom in terms of what I wanted to be working on and how I wanted to spin my story in research. I could essentially be my own boss from the very beginning.

How did serving on the ASMS Board help you to grow both personally and professionally?

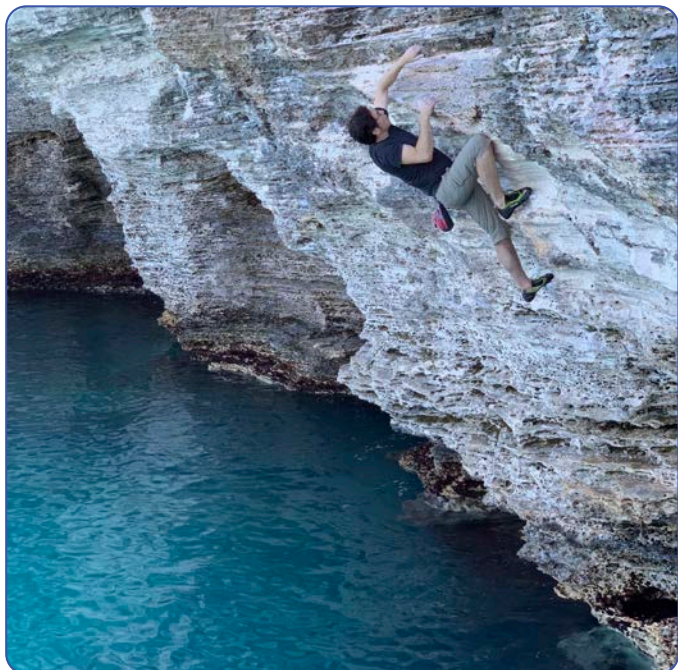
I was nominated for the board in 2013, and I started my term in 2014, which was also the year that I went back to grad school. It gave me the ability to meet a ton of people who really love the mass spec community and want to see it flourish. The people serving on the board for ASMS all care about the long-term success of the mass spectrometry community. In many ways, they care about that even more than about their research. It was amazing to meet people who saw that as a driving goal for them, and it was one of the high points of my early career. I also was involved with the board at the same time as some other very influential and important people in my life. One of the past presidents, Sue Weintraub has consistently been a guiding mentor for me, and has been a really important person in my career and my personal life in general. Vicki Wysocki was the president at the time, and is one of the main reasons why I'm here at Ohio State. She helped connect me with the right people, navigate the departments, and get excited about research at OSU. Those two people in particular had a substantial influence on my trajectory, and those relationships were cemented during my time on the board.

What type of work have you done with the Association for Biomolecular Resource Facilities (ABRF) community?

ABRF research groups are rotating teams of scientists from around the world that try to investigate technical problems that require a community of researchers to solve. Early on in my career, I was a founding member and at one point a chair of the Proteome Informatics Research Group (iPRG). We usually would pick a project designed to last for a year or two, and then release the results to the ABRF community. Many of these projects ultimately get published in peer-reviewed journals. These types of projects are usually designed around helping us understand where the community is in terms of trying to do a specific task, such as analyzing a certain type of sample or using a certain type of analysis method. I've been on and off multiple ABRF research groups for almost 10 years now, and that has definitely been an important part of my learning process. I believe these sorts of community projects are a great way to investigate problems from multiple angles, as well as to network with other like-minded researchers. I always encourage young investigators to get involved with the ABRF, even if they aren't running resource facilities of their own.

What types of problems related to cancer do you hope your work might one day help solve?

Cancer is, inherently, a genetic disease. We usually think of it as being a disease that you typically would study with genomics and transcriptomics, but many types have genetic variants have important manifestations in the proteome. Often, cancers carry many different genetic variants—hundreds of them are in tumor cells, but only a handful of them are actually really driving the cancer to grow, proliferate, and metastasize. My lab is interested in trying to tease apart which of those genetic variants are actually meaningful by studying their effects in specific proteins or across the proteome. Once we can determine which genetic variants are impactful, we can develop targeted tests or therapies toward those specific variants. These types of questions are interesting not only from the standpoint of cancer, but also from the standpoint of what makes us all a little different—for instance, how well we respond to different drugs or how specific phenotypic traits are manifested at the molecular level. Many different types of diseases are driven by specific genetic variants, but it's hard to understand why those specific variants are the drivers. That's what we're trying to get after, with cancer being one of our centerpiece questions.



Deep water soloing (rock climbing above water) at Clarence Cove in Bermuda prior to collecting ocean metaproteomics field samples at the Bermuda Atlantic Time-series Study (BATS) site in collaboration with the Saito lab. Photo credit: Julia Haskin

What are some of your current projects?

A lot of our research uses an approach called data independent acquisition mass spectrometry (DIA-MS), which lets us build more complete pictures of samples with fewer missing data points. One side of the lab is trying to develop new ways to collect and analyze that type of data. Our lab produces the open-source, freely available EncyclopeDIA software suite for analyzing DIA-MS datasets. We are currently working on approaches to improve peptide quantification, detection accuracy, and throughput using this software.

The other side of the lab is focused on applying those technologies to cancer research. Some of our recent work has centered specifically around studying viruses as drivers for cancer. Viruses that stick around in the system can play important roles in unexpected long-term diseases, such as cancer. Many people know, for instance, that some human papillomaviruses (HPVs) cause cervical cancer. There are eight known human herpesviruses (HHVs), and we already know that two of them cause cancer. For example, Epstein-Barr virus (EBV), which causes mononucleosis in most people, undergoes something called an abortive lytic pathway where it lives long term in your body. Here it doesn't just silently bide time; instead, it actually makes genes and proteins that change the host cell programming to affect survival and proliferation. Those changes to the host programming are similar to changes that drive cancer, too. We're interested in studying what happens in these types of infections.

What types of mentorship work have you done?

Teaching and mentorship have been important drivers for my career. I love trying to take complex topics in mass spectrometry and distill them down into digestible chunks while retaining the important details. It was one of the most enjoyable parts of my tenure at Proteome Software and it's the reason why I went back

to school. For me, teaching lets me reexperience the learning process—my favorite part of scientific research—through my students' perspective. I've also done teaching activities at elementary schools or science fairs as a way to engage with younger people to get them excited about science and thinking about the world around them.

Another aspect of this has been mentoring different researchers and computer programmers at the software company. We usually end up hiring programmers that have come in with no science experience or scientists with no software experience. Several have stayed within the mass spec community, refocusing their careers on mass spectrometry. It has been exciting to be a catalyst for people broadening their interests out into different areas. Part of the fun of mentoring is bringing people into my circle of contacts and interactions—giving them what I have been given. The mass spectrometry community is a wonderful group, in part because it is really interested in seeing younger scientists flourish. One of the great things about this community is its focus on making it easier for younger researchers to get involved with and excited about mass spectrometry.

What are your interests outside of the lab?

When I decided that I was going to start Proteome Software, I also decided at that point that I needed a hobby to stay sane. So, I went to the local ceramics community center just down the road from where I was living in Portland. As we were starting the company, this was kind of my stress relief technique: to go make pots at the center. That ended up becoming a really big part of my life, and I did a little art teaching and showed my work in a few galleries. The Portland art community was really nourishing for me at a time when I appreciated having a diversion. I've also done a lot of rock climbing over the last decade.

I came to Ohio thinking it was going to be extremely flat, but much of it is on the Allegheny Plateau, so you often find beautiful cliffs cut by rivers. Rock climbing is a hobby that I've been able to carry with me, and I was very pleased to be able to continue that here. Normally, I'm a terrible exerciser because I just get mentally bored. But rock climbing doesn't really feel like exercise—it's often more like a mental puzzle because you have to figure out the physics of how your body is positioned and how you can make physical movements. That helps me to think that I'm actually getting exercise.



A raku floor vase thrown and fired by Brian at the Multnomah Arts Center in Portland Oregon. Photo credit: Brian Searle