FACES OF MASS SPECTROMETRY / Mike Morris

Anne Brenner and J.D. Brookbank are science writers at Technica Editorial Services.

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It's All About the People

Mike Morris earned his PhD in mass spectrometry from the University of Manchester in 1988. After pursuing rewarding research opportunities in places such as Japan, the USA, and Canada, Mike accepted a job at VG/Micromass/Waters in the R&D department in 1994, and he has been working with this company ever since. During this time, Mike has served as head of the organization's Clinical Applications Group (1999) and as Senior Director of Mass Spectrometry Research (2010). Over the course of his career, Mike has co-authored over 70 scientific publications and has helped organize numerous mass spec conferences and society meetings. He is an inventor of over 25 granted U.S. patents and is affiliated with a number of notable professional societies. His research contributions in several clinical areas—particularly neonatal screening—have helped push mass spectrometry applications into many exciting new fields and work environments. More recently, his research has focused on advancing mass spec instrumentation and capabilities as part of the Waters Research team. In September 2024 Mike was recognised by the British Mass Spectrometry Society (BMSS) as the eighth recipient of the BMSS Medal for "sustained contributions by a member of BMSS in developing the science of mass spectrometry."

Despite a long list of personal accomplishments, it is clear that Mike does not view the arc of his career in quite these terms. Rather, he is quick to point out that his story features an extensive cast. Moreover, he firmly believes that his achievements stem from being part of a team, being in the right place at the right time, and being with the right people to be able to push things forward. He also emphasizes the importance of connectivity and teamwork—kicking ideas around with colleagues at a cafe or pub, for example—because this helps bring the knowledge of multiple parties together and can ultimately bear fruit in the form of solutions that are bigger than the contributed parts.

Did you decide to pursue graduate studies in mass spec during your undergraduate years at UMIST, Manchester, or afterward?

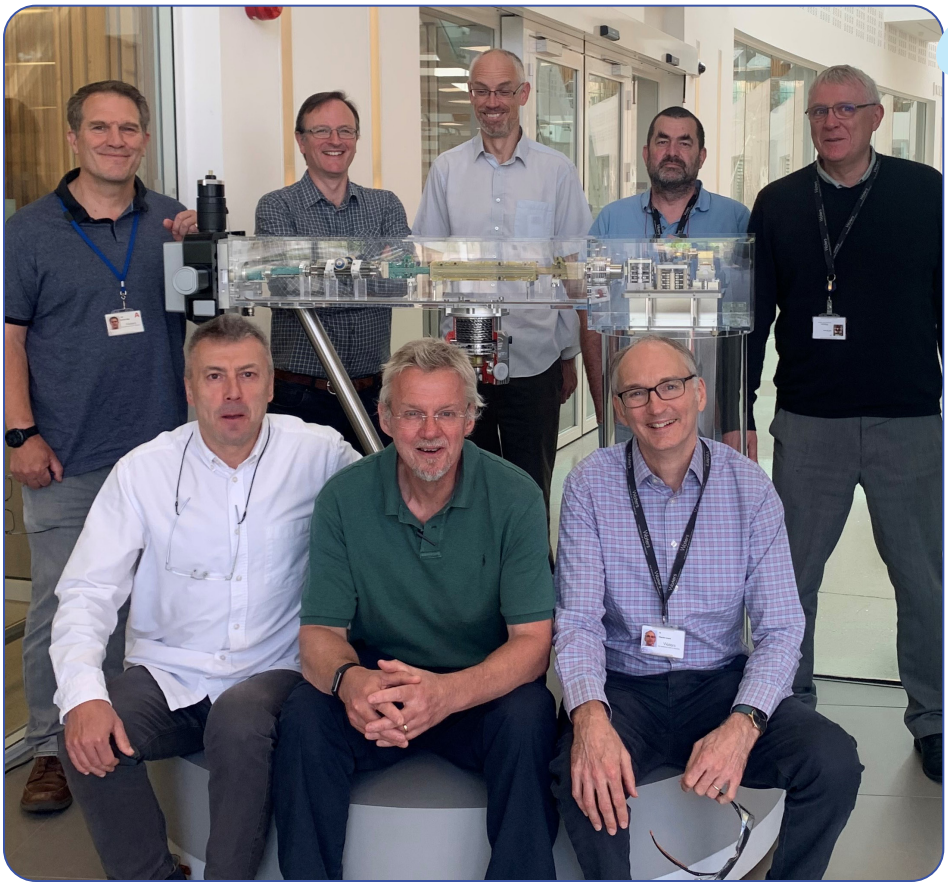
I suppose I should admit to having an interest in analytical chemistry in high school, and I went to UMIST for undergraduate studies as it was (in 1982), one of only two universities in the U.K. offering Analytical Chemistry as a degree subject.

In my final year, I took a course labeled "analytical instrumentation," and for the first lecture (there were only a dozen of us) The tutor ambled into the seminar room, sat on a desk at the front, and started chatting about analytical instruments. I was hooked from that date. The lecturer was Michael (Mickey) Barber.

As we approached final exams, I was doing a project with Mickey. I had received a job offer from Glaxo, and he suggested we go for a beer and a chat, which was quite a regular feature of working in his research group. In the next hour, he convinced me to study for a PhD with him so I could "meet the people who were writing the papers I was studying"—he wasn't wrong, and it changed my life.

I started in Mickey's group in 1985, and I worked in his team until his passing in 1991. The focus was on the implementation of tandem mass spectrometry on the study of biological molecules using fast atom bombardment ionization. We were extremely fortunate to be based in Manchester where two major instrument manufacturers (Kratos and Vacuum Generators (VG) were located. We spent a considerable amount of time in these factories running experiments. We were also fortunate enough to interact with local groups at ICI that were within easy traveling distance of the university and had purchased "modern" instruments that they allowed us to use.

As part of my PhD studies (1986-7), I was privileged to spend a year in Osaka studying ion optics with the group of Takekiyo Matsuo (Hisashi Matsuda, Itsuo Katakuse, and Toru Sakurai) and worked on a new JEOL instrument for high mass analysis (clusters) using ion gun bombardment. This was a massive instrument (9 tonne magnet), and we burned through ion gun electrodes at the rate of one every



> *With connectivity, ideas can be discussed, challenged, developed and realized, or discarded.*

Some of the Waters Wilmslow Research team in front of a (non-working) model of a Synapt mass spectrometer. Back (L-R): Kevin Giles, Keith Richardson, Dave Langridge, Steve Pringle, Jeff Brown. Front (L-R): Steve Bajic, Mike Morris, Martin Green. (Photo courtesy of Mike Morris.)

two days to study clusters up to m/z 10,000. The following year (1988), electrospray made an entrance at ASMS and IMSC, and this opened the study of large biomolecules without the need for high-mass range instruments owing to the multiply charged nature of the analytes.

We understand you joined Micromass/Waters in the R&D department in 1994 after completing positions in Japan, the USA, and Canada. Can you tell us about the transition from academia to industry?

At the end of my time in UMIST (late 1991), we hosted an international meeting on tandem mass spectrometry, and one of the invited speakers was Graham Cooks. We had a discussion, and I asked if he had any post-doc positions available. The result was that I spent a fulfilling 12 months in West Lafayette, Indiana working on surface-induced dissociation.

Following that, I went north and spent two years in Bob Boyd's group at the Canadian National Research Council in Halifax, Nova Scotia. This was my first foray into electrospray ionization—considerably "easier" than FAB (Fast Atom Bombardment) for routine analysis and potential automation.

In early 1994 when my second child was due, the search for my next career move had started, and my wife was keen for us to settle somewhere for a while. Before we left England, I had received an approach from VG, and I decided to pursue this option. I started at VG Biotech as part of the R&D team, assigned as Brian Green's "assistant". Concerns I might have initially had about the scientific relevance of the work within a commercial organization were soon dispelled. Brian was heavily focused on scientific rigor, and we also had the opportunity to work on customer problems that were often far from routine. Having access to a factory full of instruments was a significant advantage, and we could juggle a number of interactions at any one time. It was at VG Biotech that Brian and I ran our first neonatal blood spot extracts for the team at Duke University; I was assigned to the project from within the R&D team as I was the lone chemist among a group of physicists and engineers. It was also at this time that we developed ideas for the study of variant hemoglobins leading to the study of over 300 different variants (e.g., Sickle, HbS)

Within the team at Micromass/Waters, there is a lot of invention that is done to advance the performance and capability of the instruments that we make. While the team does collaborate with folks outside the organization, many of the inventions and advances come from within. One respected U.S. academic, when visiting the factory, was surprised at the novel science being developed, as prior to the visit they had thought that the manufacturers just commercialized ideas that had been published in the literature rather than initiating the inventions themselves.

How did you decide to focus specifically on mass spec as it applies to the health sciences realm?

In all the projects I have been involved with throughout my career, I have always looked for the "relevance" of the science. Looking at problems where we could study the structure of drugs, metabolites, and compounds of life science relevance was easy to justify, especially if there was a disease-related impact.

> *It has been all about the people as much as the science—the friends, colleagues, collaborators, students, post-docs, academics, and industrialists.*

Hiking in the countryside at Seven Falls, near Tintwistle, Derbyshire, U.K. L-R: Kevin Giles, Steve Pringle, Mike Morris, Keith Richardson, Martin Green. (Photo courtesy of Mike Morris.)

With regard to your current role at Waters in the U.K.: What originally drew you to this company and this position?

My contract in Nova Scotia was coming to an end, my eldest child was approaching school age, and my second child's arrival was imminent. Returning to the U.K. was our plan, and I needed a job. I knew people at VG, because I had met them at international gatherings, such as the ASMS meeting. Also, the company was located in an area of the U.K. that we knew well. The original job was in R&D, but it ended up being far more wide-ranging. Detailed job descriptions were not high on the agenda in the mid-90s!.

We understand you founded the Clinical Operations Group in Waters in 1999. What has it been like to see this group evolve since then?

I worked on the implementation of neonatal screening from the first experiments and installation (Duke, 1995) and was involved in the presentation of the work at meetings where mass spectrometry would not typically be present (e.g., SSIEM, Society for the Study of Inborn Errors of Metabolism; ISNS, International Society for Neonatal Screening).

We were at a meeting in Turku, Finland in June 1999, and I went with a colleague (Don Cooper) to the conference dinner—we were woefully under-dressed for the occasion—jeans and T-shirts when everyone else was in dinner dress! We skulked in a corner with a couple of beers and hatched a plan to try to make more use of mass spectrometry in the routine clinical space. The following evening (in Stockholm), we sat on a street café with the head of pathology at Manchester Children's Hospital, Mike Addison, and chewed the fat over what assays might benefit from the specificity of mass spectrometry and followed up with a visit when we got back to Manchester. One of the problem assays was for monitoring tacrolimus (an immunosuppressant drug) in transplant patients and the issues (at the time) of cross-reactivity of the immunoassay with metabolites. We asked Mike if he could provide some samples, and he referred us to Wythenshawe Hospital (University Hospital of South Manchester), which was located (literally!) just across the street from our factory and was a regional center for transplantation. A phone call later, we had a talk with the Consultant Biochemist, Brian Keevil, and he walked over for a coffee and a chat. This really started a long-term collaboration that allowed us to test the utility of LC-MS(/MS) across a variety of assays to augment the focus we had initiated with newborn screening.

With the efforts of Therese McKenna and the group at Manchester Metropolitan University, we also explored the use of MALDI-MS in the identification of bacterial cultures, and, along with Michelle Wood, explored the use of LC/MS(/MS) in clinical and forensic toxicology. The clinical applications group was formalized in Micromass (U.K.) in 1999 by Norman Lynaugh, and it was recognized as an entity within Waters in 2002.

Clinical Mass Spectrometry in Waters has developed significantly since those early days, and various changes of management have brought different levels of focus to different parts of the business. The underlying principle of "do good science" remains fundamental.

Are there any emerging health science applications of mass spectrometry that you are particularly excited about?

The area that excites me at the moment is the transition from clinical mass spectrometry to medical mass spectrometry and bringing the technology closer to the patient. The work done in some of the clinical labs, as well as in many hospitals and private organizations, has brought mass spectrometry to a fantastic level of acceptance in the clinical analysis arena. The challenges from the manufacturers' perspective were that these were a different group of customers with different levels of expectations as to what the technology might routinely and reliably deliver on a 24/7 basis, in addition to the regulatory requirements that needed to be met.

I would also recognize the group that founded the Mass Spectrometry & Advances in the Clinical Lab (MSACL) organization in 2005 to promote the use of mass spectrometry in the clinical laboratory, as well as the Association for Diagnostics and Laboratory Medicine (ADLM, formerly AACC) for supporting the introduction of LC/MS(/MS) into the routine testing environment.

The technologies that are being explored at the moment using direct ionization might have relevance in real-time or near real-time applications such as surgery or pathology. Imaging capabilities have also advanced significantly in recent years, and the potential for Desorption Electrospray Ionization (DESI) imaging with AI data analysis could be another exciting endpoint.

How has your role on various committees, such as the BEIS Program Expert Group—Chemical and Biological Metrology, helped you grow as a mass spec professional?

My interactions with various groups and committees have been excellent for forging connections across academia and industry in forums where science can be discussed both formally and informally. It's not just one-way in terms of education—there have been a lot of people who have helped me understand things to allow me to better contribute to the problems we're trying to solve (Figure 1). Connections allow you to develop and learn, which I think is good for all professionals, regardless of discipline.

As you mentioned, I am particularly proud of my invitation to join the BEIS (U.K. Government Department for Business, Energy and Industrial Strategy) Program Expert Group—Chemical and Biological Metrology, which I have been a part of since April 2018. My role in this group is to contribute to the team that makes recommendations on topics to the U.K. National Metrology Group related to chemistry and analytical measurements—it was a privilege to be invited to contribute to their efforts as an industrial representative.

I am proud to have been a member of the British Mass Spectrometry Society since 1986 and have served two periods on the Committee, and am currently Vice Chair of the Society. (BMSS is, allegedly, the oldest MS Society in the world, celebrating its 60th anniversary in 2024!)

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We understand that you have focused heavily on mass spec as it pertains to neonatal screening. How has this helped to combat disease in infants?

Inherited metabolic diseases are relatively rare in themselves, but with the full menu of disorders that can be tested using a single MS/MS analysis (50+ diseases in approximately 2 minutes) from what equates to around 200 nL of whole blood or less (depending on the sampling protocol), the overall incidence of all disorders is around 1 in 5,000. In the U.K., there are approximately 700,000 live births per year, which means that you could potentially influence and affect the lives of around 140 children (and their families) every 12 months. In the U.S., there are between 3.5 and 4 million live births per year, and the potential impact is proportionally higher. Obviously, this depends heavily on local legislation about which disorders may be tested for and which treatments are available.

The recognition, however, must go to the labs themselves—particularly those that saw the potential in the very early days—along with the public health programs that first implemented the technology on a statewide or national scale.

Do your interests outside the lab include any interesting hobbies?

My interests outside the lab are varied, and they are mostly related to family—specifically my children and grandchildren. I enjoy exercise (squash, swimming, and skiing) —mostly as an "enthusiastic amateur"! In the past, I have had a good time scuba diving with friends, although at present this is restricted to the relative chill of British quarries and coastal waters. We are fortunate to live in the Peak District in Northern England, and we have easy access to the open countryside (Figure 2), where we spend a good deal of time hiking.

Final thoughts?

It has been all about the people as much as the science—the friends, colleagues, collaborators, students, post-docs, academics, and industrialists—far too many to list here. (And I would probably forget some, too!) (Figure 1.) My career, while not over just yet, is probably in the final phases. The science we have been able to pursue, and the fun I have been able to have with those folks over the last 40 years, is what has made everything worthwhile!