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EXPERIENTIAL EDUCATION: MASS SPECTROMETRY ENTERS THE TEACHING LABORATORY

Mass spectrometry is on the rise. As the use of and applications for mass spectrometry continue to accelerate, so will the number of careers that require expertise in these tools. Historically, many undergraduate students graduated with a degree in chemistry without ever touching a mass spectrometer. Chemistry students had to settle for learning the theory of mass spectrometry in a lecture hall and handing samples over to a technician for analysis when in the teaching laboratory.

The global mass spectrometry market is expected to grow 7.6% each year, to reach more than $10.5 billion by 2025, according to a recent report by the Market Research Engine.[1] All these new instruments will need to be designed, built, and maintained, and their users will need to understand the data and how to get the best out of their tools.

Thanks to the diminishing size and cost of mass spectrometers, coupled with their increasing robustness and ease of use, universities are now starting to furnish their undergraduate chemistry laboratories with this advanced analytic tool. "My favorite learning environment is the laboratory," explains Paul A. Flowers, professor of analytical chemistry at University of North Carolina at Pembroke. "I like teaching students fundamentals through bona fide research experiences." Flowers began using mass spectrometry in the teaching laboratory about six years ago and hasn't looked back.

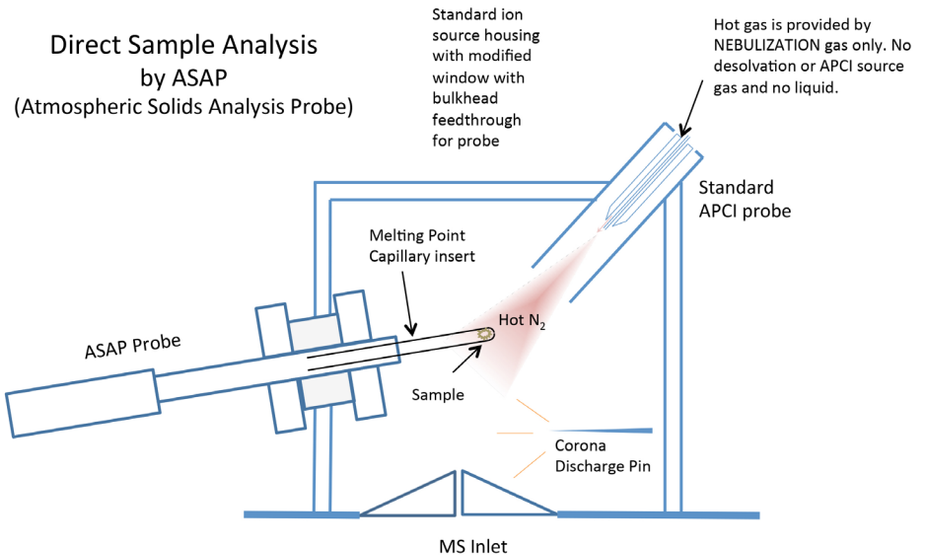
Nowadays, increased pharmaceutical R&D spending, a growing petrochemical industry, and a governmental focus on environmental testing, drug safety, and food quality are all significant contributors to the continued expansion of mass spectrometry. Newer applications for mass spectrometry, including those in clinical diagnostics, the legal cannabis market, and homeland security are fueling additional growth, as is a need for chemical analysis in remote locations—such as in outer space.

Through hands-on experience with instruments "students learn how the data is generated and not to just take it at face value," explains Blánaid White, associate professor in analytical chemistry at Dublin City University, in Ireland. "They also gain a better understanding of the fundamentals."

TRAINING FUTURE ANALYTICAL CHEMISTS

Mass spectrometry is a workhorse in diverse environments, from the pharmaceutical industry to law enforcement. To provide a taste of this diversity, Flowers coaches students in his senior-level courses to use mass spectrometry in determining the active ingredients in medications and in identifying unknown explosives.

His teaching laboratory houses an Advion expression compact mass spectrometer (CMS) and a direct analysis probe, known as the ASAP (atmospheric solids analysis probe). The probe uses the instrument's atmospheric pressure chemical ionization (APCI), eliminating the need for students to carry out any sample preparation before analysis.

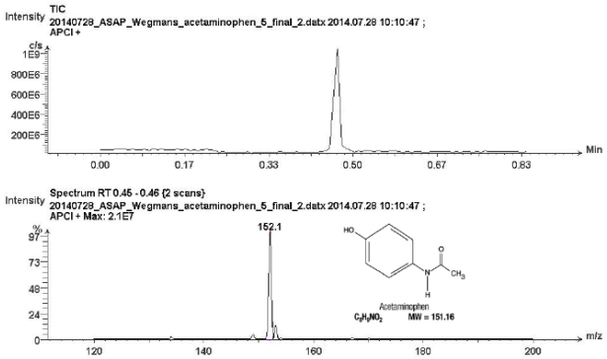


A schematic of the atmospheric solids analysis probe (ASAP).

Image credit: Advion

"The Advion expression CMS is a super nice instrument," Flowers says. "The APCI ion source with an ASAP sampling probe allows for direct insertion of liquids and solids, making for very quick analyses." Each analysis typically takes 30 s or less. "In our larger-enrollment, lower-level labs, we can get a lot of students in and out quickly," he adds.

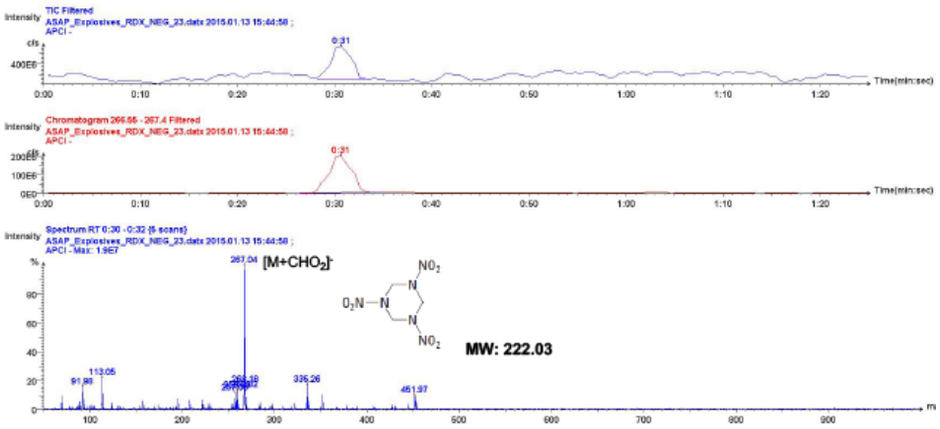
The students use the instrument to identify active ingredients in over-the-counter painkillers. For example, a migraine medication "has three easily identified components—caffeine, acetaminophen, and aspirin," Flowers says.



Example 1: An easily identified peak for acetaminophen was found using a positive ion ASAP/CMS analysis of a tablet.

Image credit: Advion

The students use the same setup to examine an unknown explosive on a glass fragment. Spectra are collected from four standards—the explosives nitroglycerin, pentaerythritol tetranitrate (PETN), hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX), and 2,4,6-trinitrotoluene (TNT)—and compared to the spectra of the unknown explosive.



Example 2: Similar to the acetaminophen example, an explosive compound such as RDX is easily detected when using the ASAP/CMS analysis method. For the full application note, read "Screening of Explosive Residues without Sample Preparation Using a Direct Sample Analysis Probe on the expression CMS."

Image credit: Advion

To let the students delve deeper into mass spectrometry itself, Flowers runs an instrumentation-focused experiment that introduces the basic principles of mass spectrometry. This class uses caffeine as its test substance and explores electron ionization (EI) mass spectrometers. The students experiment firsthand with the two types of ionization sources, EI and APCI, investigating the effects of various instrumental parameters on spectral quality.

Students also have the opportunity to carry out more in-depth research projects using the expression CMS. "Students in our instrumental analysis course spend several weeks working on individual lab projects. One recent project explores the use of internal standards to improve the precision of ASAP measurements," Flowers says. Projects like this put the full spectrum of mass spectrometry sampling, testing, maintenance, and calibration directly into the students' hands.

At Dublin City University, third-year analytical science students gain hands-on experience with a gas chromatography/mass spectrometry (GC/MS) instrument. Experiments include identifying hydrocarbon pollutants in soil samples and comparing generic and branded nonsteroidal anti-inflammatory drugs.

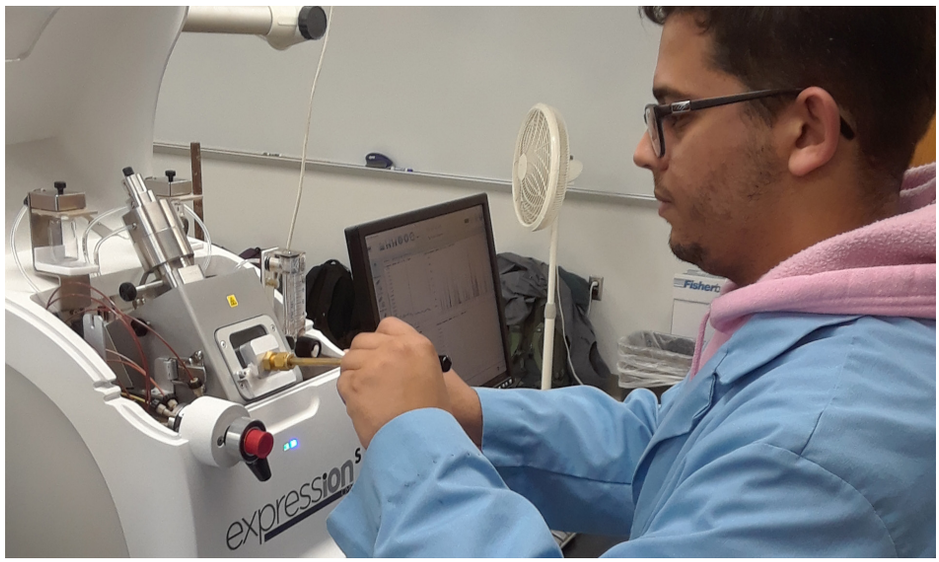
The Dublin students also explore mass spectrometry fundamentals such as techniques for preparing samples that optimize the data obtained by the instrument. “They compare a couple of derivatization agents and see how that what they do to a sample as part of its pretreatment can have such a massive impact on the signal that’s generated at the end,” White says.

“Then in their final year, because they’ve got the experience and the training on it in third year, our students have a suite of instrumentation available to them to use during a research project,” she explains.

The pharmaceutical industry is the main employer of Dublin City University’s analytical science students. “In Ireland, we have a huge number of the big pharma companies with manufacturing plants. So a lot of our students do go directly into those plants,” White says. They take up roles such as quality control analytical chemist, process chemist, and production chemist.

Chemistry majors at Wilkes University use an expression CMS as part of an experiment designed to provide hands-on experience of validating a high-performance liquid chromatography (HPLC) column.

HPLC column manufacturers provide certificates that state the elution times of certain compounds, under certain conditions. It’s important that users test the performance of their columns against the manufacturer claims, to ensure accurate analyses.



Undergraduate student Jose Acosta, University of North Carolina, using the expression CMS to investigate the precision of the ASAP probe for analyzing aqueous caffeine.

Image credit: Paul Flowers

"I want my students who leave here and go to work for industry to understand that you need to periodically evaluate the column performance," says Donald E. Mencer, associate professor of analytical chemistry at Wilkes University.

The 300-level students in his lab make up samples containing four or five components. "We've got a small post-HPLC column splitter valve that after the sample runs through the HPLC column we split about 0.8 mL/min to the UV detector and the other 0.20 mL/min to the mass spec detector," Mencer explains. "They collect data in both data channels and learn a little bit about the different sensitivity of the mass spec detector and that not all molecules ionize equally efficiently."

For this experiment, the students are using an electrospray ionization source on the expression CMS. Wilkes University also has an ASAP that is used for undergraduate research projects. "It's pretty easy to switch the electrospray ionization source that we tend to use when it's hooked up to the HPLC over to the APCI if we want to use the ASAP probe. It only takes a few minutes," Mencer says.

"One of the things I like about the CMS is that it's not intimidating at all to students. You can pretty quickly get them past any initial fears about picking apart hardware and putting in pieces and reconfiguring the plumbing," he adds.

TRAINING PROSPECTIVE END USERS

Mass spectrometers are also starting to find a home in organic chemistry teaching laboratories as a routine tool for verifying identities of synthesized molecules.

When a student obtains unclear data from infrared and nuclear magnetic resonance (NMR) spectroscopy for their synthesized product, "We can now say, 'Let's put it on the mass spec and see if we can find any of your compound in your mixture,'" explains Andrew Worrall, deputy director of chemistry teaching laboratories, University of Oxford, UK. "From deciding we want to do it to getting the results takes a couple of minutes."

In September 2018, the University of Oxford opened new chemistry teaching laboratories with a multimillion-pound analytical suite. It houses an expression CMS, alongside other state-of-the-art instruments such as a benchtop NMR spectrometer.

Oxford students use an ASAP to check the identity of their molecules. The new analytical suite also hosts a Plate Express TLC (thin-layer chromatography) plate reader for the expression CMS; this setup is often referred to as TLC/CMS. In less than a minute, this setup collects mass spectrometry data from a spot on a developed TLC plate. Within seconds, the TLC/CMS system is ready to run another sample.

"We use the TLC mass spec in an experiment where students extract caffeine from a natural product, like tea," Worrall says. "The students do a crude extraction, run a TLC on the crude extract, and then use the TLC mass spec to identify which part of the TLC contains caffeine." From this, they can optimize the design of the purification step.

The Plate Express TLC plate reader for the expression CMS collects mass spectrometry data from a spot on a developed TLC plate.

Image credit: Advion

This experiment is an example of the shift away from the traditional cookbook approach to teaching labs. "We're moving away from telling students to follow a recipe, where they are basically technicians. We want to train them to become research scientists," says Malcolm Stewart, director of teaching laboratories, department of chemistry, at Oxford.

"Introducing undergraduates to expensive pieces of [equipment] also gets them ready for the high-tech environment during their fourth-year research project with one of our research groups," Worrall adds.

The college of pharmacy at Purdue University also introduced a TLC/CMS to its undergraduate organic chemistry laboratory in the fall of 2018. This was the fourth expression CMS purchased by the university; it already had three in use for research.

The expression CMS ASAP probe allows for the direct insertion of liquids and solids, with no sample preparation required.

Image credit: Advion

"When I saw the user-friendly interface, how quickly data was collected and how easy it was to analyze the data, I thought it was the easiest mass spec that I'd ever used," says Daniel P. Flaherty, assistant professor of medicinal chemistry at Purdue University. Flaherty also thought TLC/CMS could really help improve the undergraduates' understanding of both mass spectrometry and compound characterization in organic chemistry, he says.

Previously, students were given printouts of mass spectrometry data and asked to tell their instructors what the molecule was. "Now, they can go and collect their own data on the molecule," Flaherty says. Purdue students currently analyze the data on the instrument itself, but there are plans to enable the data to be accessed remotely via the Advion Data Express processing software, as each student can download and access the software from his or her own computer. The department already has a system in place that is used with other analytic instruments.

"The students use the instrument to collect the data, put the data on a flash drive, and then take it back to their workstation and analyze it there," Susan R. H. Holladay explains. Holladay is the director of undergraduate laboratories at Purdue. "That is the model that we're going to use for the Advion mass spec next time we teach with it."

Last year, Purdue started using TLC/CMS in a nitration experiment for sophomores in its teaching laboratory. "The reason we found the need for the TLC plate reader with this nitration experiment is because the products can be nitrated more than once," she says. Historically, melting points and infrared analysis of the product hasn't always given a clear answer as to the product obtained. "By using the mass spec, they can quickly and clearly see what the mass of their product is," Holladay says.

"One of the things that we work hard on is making sure that we don't have just cookbook laboratories," she adds. "We don't want the students to just show up, make a substance, verify the substance, and then go, 'Oh, look, we made what we thought we made!' We, therefore, give our students different starting materials. So, they're doing the same experiment, but getting different products."

Flaherty and Holladay now plan to introduce the TLC/CMS to a number of other organic chemistry teaching laboratory experiments for which there's not a clear-cut answer as to what the product might be. "We try not to use an instrument just to use an instrument," Holladay says. She, Flaherty, and others try to make sure that its use is helping the students in their learning, she adds.

Looking to learn more about TLC/CMS? Download the application note, "Suzuki Reaction Monitoring Using Compact Mass Spectrometry with the Plate Express TLC Plate Reader."

CONCLUSION

Inexpensive compact mass spectrometers are expected to continue their charge into university teaching laboratories, where their speed, usability, and robustness are enabling—in many cases, for the first time—undergraduate students to have hands-on experience with a research-grade instrument that they are increasingly likely to encounter if they progress through a scientific career. The lessons learned from an experiential education in mass spectrometry will be with them every step of the way.

REFERENCES

1. Market Research Engine, *Mass Spectrometry Market by Platforms Analysis (Hybrid Mass Spectrometry, Single Mass Spectrometry); by Application Analysis (Pharmaceuticals, Biotechnology, Industrial Chemistry, Environmental Testing, Food & Beverage Testing) and by Regional Analysis—Global Forecast by 2018-2025* (Deerfield Beach, FL: Market Research Engine, December 2018), https://www.marketresearchengine.com/mass-spectrometry-market.

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