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State-of-the-art mass spectrometry for point-of-care and other applications: A hands-on intensive short course for undergraduate students

Patrick W. Fedick, Ryan M. Bain, Shunshun Miao, Valentina Pirro, R. Graham Cooks*

Department of Chemistry and Center for Analytical Instrumentation Development, Purdue University, West Lafayette, IN 47907, United States

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ABSTRACT

Current mass spectrometry techniques and applications, especially those which achieve high speed by using ambient ionization and/or miniature instruments are presented with emphasis on the nature of the instrumentation and methodology. This is done in the context of describing an intensive two-day workshop for upper division undergraduate students (9th annual meeting for the Center for Analytical Instrumentation Development, CAID, Purdue University). Six hands-on demonstrations are detailed. Multiple ionization sources, types of mass spectrometers, and ion manipulation techniques are covered. The meeting "State-of-the-Art Mass Spectrometry for Point-of-Care and other Applications" might serve as a model for intensive short courses that other institutions might wish to develop in their particular research specialties. A hallmark is the emphasis on methodology, fundamental theory, and current applications. The effectiveness of the CAID short course to deeply immerse, motivate, and educate students was confirmed through formal student assessment and feedback.

1. Introduction

Mass spectrometry is a core component of many chemistry curricula, with in-depth coverage often occurring in analytical chemistry courses [1]. Mass spectrometry, however, is often introduced in an undergraduate student's first year, as seen in the American Chemical Society's Anchoring Concept Content Map of General Chemistry [2] and Organic Chemistry [3] and a number of laboratory exercises targeted at these students [4–6]. While there is no formal Anchoring Concept Content Map for Analytical Chemistry, one would imagine that mass spectrometry would be a 'level one' anchoring concept and that ionization sources would be considered an important component.

Ambient ionization was first reported in 2004 with the introduction of desorption electrospray ionization (DESI) [7]. DESI-MS requires solvent to be sprayed, using an electrospray, at a surface on which analyte is present. The impact of charged solvent droplets on the surface generates secondary droplets which carry the analyte from the surface into the mass spectrometer [7]. In the 13 years since the first publication on DESI, ambient ionization has expanded rapidly and is the topic of a number of reviews and books [8–14]. Traditionally, students are taught the fundamentals of mass spectrometry in undergraduate courses, however, emerging techniques are typically omitted [8]. With course and laboratory time being limited, especially in a course such as Instrumental Analysis where a plethora of instrumental techniques are often covered, topics such as ambient ionization may not get sufficient coverage, if they receive any [1].

With mass spectrometry now so crucial to analytical chemistry courses, as well as being an important tool for most chemists and biologists, Purdue University's Center of Analytical Instrumentation Development (CAID) has been holding two to three-day graduate student organized workshops open to internal and external students since the summer of 2008. This workshop has become a set piece in Purdue's undergraduate Instrumental Analysis course, where students get firsthand experience with recent mass spectrometry developments while reinforcing the fundamentals learned in the classroom. The assessment exercise developed as part of this short course, focused on students registered for Instrumental Analysis at Purdue University, but students from other courses, other universities, and industrial scientists also attend the CAID workshop. Similar to chemistry summer camps [15,16] and short courses [17] which blend hands-on research, lectures, and discussions of chemistry over meals, the annual CAID meetings attempt to showcase novel research while covering the fundamentals. Students were guided through CAID by graduate students, who are currently performing research on these topics, through a peer led style that contrasts with traditional course structures [18]. This allowed the students to become comfortable with the advanced materials and facilitated questions about the material.

CAID provides an out of the classroom, hands-on period for the students to experience mass spectrometry and learn about recent advances in the field. CAID takes the fundamentals learned by the

* Corresponding author.
E-mail address: cooks@purdue.edu (R.G. Cooks).

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students in the classroom and provides a "crash course" on relevant applications, information on how to operate the instrumentation, and a firsthand look into new areas of research in mass spectrometry. The goal of this paper is to give an overview of how CAID has been developed and is run, while encouraging other universities to develop their own CAID style workshop as a beneficial educational tool, with emphasis on their own particular research fields.

2. Experimental

2.1. Analysis of human brain cancer using tissue smears by desorption electrospray ionization—mass spectrometry

The first hands-on demonstration began with graduate student, Clint Alfaro, discussing some of the recent efforts in human brain cancer diagnosis by DESI-MS [19]. The students first learned the fundamentals of DESI-MS [7], from how the analyte ions are created, all the way to the production of a useful image [20]. Students were then shown past data of human brain cancer images and learned how DESI-MS is potentially a useful tool in the operating room complementing information from histopathological examination [19]. Students were then provided the 3D printed tissue smear device [21] and a section of mouse brain to prepare for DESI-MS analysis. They were walked through a variety of negative and positive ion scans that they then performed. Each specific scan targeted a different subset of compounds: lipids, metabolites, or particular targeted analytes (Fig. 1). The students were instructed on what could be learned by each of these scans, such as differentiation between gray and white matter, and the presence of gliomas, meningiomas, and pituitary tumors, as well as how multivariate statistical analysis provided the capability to differentiate cancer from non-cancerous brain matter.

2.2. Biofluid analysis by paper spray mass spectrometry

The second hands-on demonstration was led by Karen Yannell and covered the fundamentals of quantitative mass spectrometry. Students were first introduced to the basics of triple quadruple mass spectrometers and how tandem mass spectrometry is performed using this particular instrument. They also learned about paper spray ionization [22], how biological matrices complicate typical analyses, and how to properly set up a paper spray ionization experiment involving whole blood (Fig. 2a) [23]. The students were instructed on how to construct a calibration curve, what quality controls are and how they are utilized in quantitative mass spectrometry [24]. Acetaminophen in human plasma (Fig. 2b) was analyzed by paper spray ionization by the students and they determined its concentration in unknown samples. Paper spray ionization was demonstrated as a suitable method for point-of-care clinical samples [25].

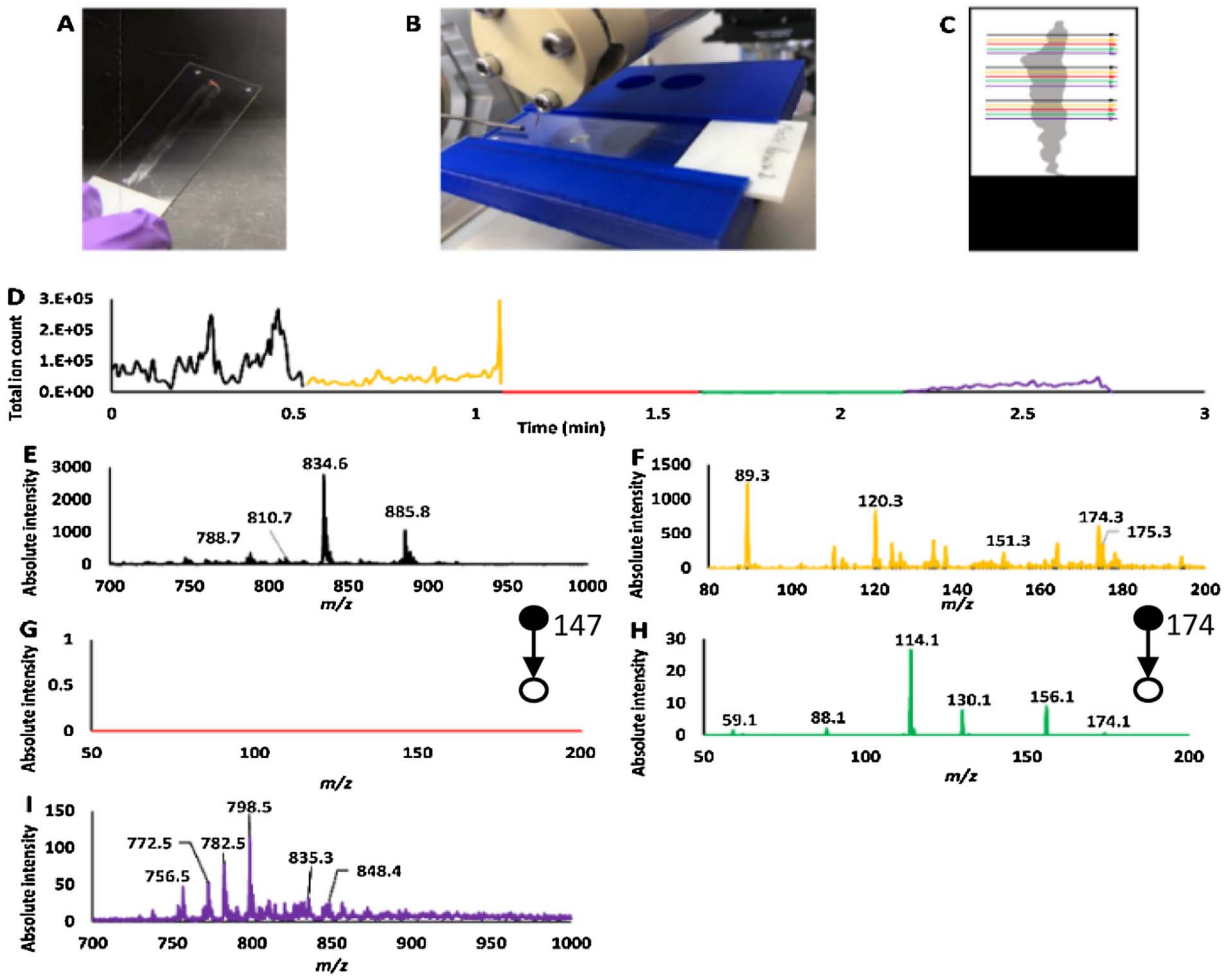

Fig. 1. DESI-MS analysis of mouse brain tissue smears performed by the CAID participants. The mouse brain smear was prepared (A–B) and data acquired (D–I) by the CAID students. A) A portion of mouse brain tissue (1–2 mg) was smeared on a glass slide. B) The sample was placed on the DESI ion source. C) The DESI spot was scanned across the surface of the mouse brain smear fifteen times, collecting five different data sets. three times for each data set. D) The total ion current recorded for the tissue smear analysis. Each color coded region represents one of the different data sets. E) Negative mode lipid profile (0–0.5 min). F) Negative mode metabolite profile (0.5–1 min). G) Product ion spectrum of *m/z* 147 (2-hydroxyglutarate). H) Product ion spectrum for *m/z* 174 (N-acetyl aspartate). I) Positive mode lipid profile.