



Curriculum, Undergraduate Research and Social Responsibility

Leveraging matrix-assisted laser desorption time-of-flight mass spectrometry to enhance student awareness of coursework relevance

by Jen Grant

Ultimately, faculty have the responsibility to tune the undergraduate degree process with student success in mind, with the aim of producing well-educated science, technology, engineering and math (STEM) graduates who thrive in the increasingly complex, rapidly changing technological environment we live in. One step in the right direction is to consider holistically how the individual student interacts with the science curriculum. It isn't enough just to add coursework to cover the changing face of STEM research, and it isn't effective to ask undergraduates to pursue research as just another add-on activity that looks good on a resume.

It's important for each STEM faculty to consider his or her undergraduates' curriculum, understand how the curriculum interfaces with the research goals of the mentor, and give students repeated opportunities to relate what might look like esoteric concepts to hands-on activities they approach in the laboratory, and to demonstrate that applicability as it plays out in the real world as a societal benefit.

My first summer undergraduate research experience following my freshman year in a prominent genetics laboratory in Madison, WI, sums up the challenges students experience today as they attempt to define their career. The first day, I was asked to degas a solution of acrylamide before pouring a polyacrylamide gel electrophoresis (PAGE) gel. The senior scientist gave me the equipment, which included an aspirator hooked up to a weak vacuum created by movement of water, and then watched me like a hawk. She wanted to know if I had had a practical education in chemistry and knew enough to remove or separate the aspirator from the vacuum connection before turning off the vacuum. Well, I did, and since then, I've been attuned to the fact that students need professional knowledge to succeed in a competitive academic and post-collegiate environment.



We, as academics in higher education, are experiencing a “perfect storm” in education. Students are challenged in many ways in college: academically, socially and career-wise. We have heard how student debt is the “next economic bubble.”¹ Many universities are striving to create three-year curricula to meet the anticipated needs of students.² At the same time, many faculty are wondering how to cram a meaningful program of study or major into a traditional four-year timeframe, while still supporting the professional, ethical and personal maturity of students. Complicating this is the nationwide, and often severe, tightening of collegiate budgets.

In its *Bio2010* report,³ the National Research Council emphasized that the majority of undergraduate science courses are mired in the procedures and curriculum of the past, leading to students who feel disengaged and even adrift. Participation of undergraduates in research is highly lauded in this report as a way to engage students and ensure they receive exposure to modern science.

The President’s Council of Advisors to Science and Technology went even further, recommending revision of the first two years of an undergraduate’s college experience “by replacing standard laboratory courses with discovery-based research courses.”

Indeed, undergraduate faculty in science have largely embraced undergraduate research as an engagement tool, and many undergraduate programs offer capstone courses that require students to perform mentored research. Unfortunately, undergraduate research is often presented as an add-on in an already complicated educational environment.

There are no short-term fixes to the present curricular issues. Instead of designing more add-ons, my approach has been to rethink how to strategically engage students so they realize the relevance of the present curriculum to the mentored research. In response, I’ve crafted a scientific research experience for undergraduates that revolves around the use of matrix-assisted laser desorption time-of-flight mass spectrometry (MALDI-TOF MS) to solve questions of medical and biological importance.

This isn’t a one-shot affair. The students in my research laboratory, who are applied science majors, are required to engage in the concepts behind the instrumental method, a



process that is designed to give them a deep appreciation of their required courses. They attend lab meetings and journal club activities. On a weekly basis, and often a daily basis, these students are exposed to discipline-specific terminology, are required to visualize the molecular processes that underpin detection using MALDI-TOF MS.^{4,5,6} Students are challenged to actively use sophisticated, professional problem-solving skills to solve problems of importance to human health. After the course of the semester, these students have shown an increased appreciation for why they need to take basic chemistry, math and physics courses.

MALDI-TOF MS is indeed an ideal instrument for including in this paradigm of intense, hands-on and “minds-on” scientific experience. MALDI-TOF MS is a prime example of a convergent technology, the study of which reinforces skills that students will need to survive in STEM. Math, chemistry math, practical (simple) statistics, basic physics and basic chemistry can all be harnessed to solve questions relevant in either biology, chemistry or both, and in a way that allows students to experience major instrumentation, develop confidence and acquire a STEM professional’s vocabulary.

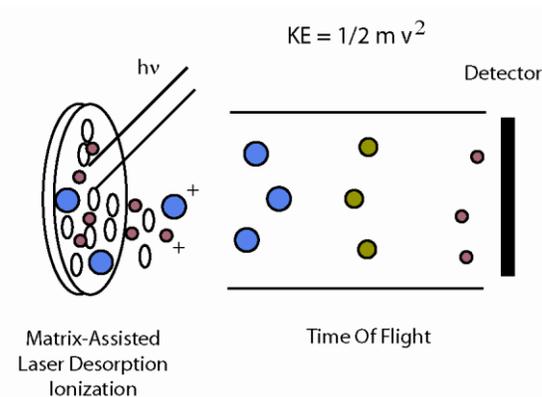
Problem-solving is highly valued when engaged in research involving MALDI. For example, students in my laboratory often must figure out how to dilute a sample to generate the best MALDI signal. Or they may be required to determine the most effective way to remove salts from a sample. Every project is unique, but ultimately returns to fundamental physiochemical concepts relevant to MALDI-TOF MS, including sensitivity, accuracy, resolution and sample preparation.

In short, strategic use of MALDI research as a vehicle for educating students requires students to keep current in basic chemistry and physics concepts and methods, as well as basic scientific practice. During the course of a semester or a year, I have seen students progress to an educational landscape where they are fluent in these STEM topics and approaching a level where they could easily translate this to a graduate-level environment

Connections between chemistry, physics and math

The fundamental principles behind MALDI TOF MS involve ion chemistry and principles of time of flight, which involves the relationship between mass, velocity and kinetic energy. It's particularly true for MALDI-TOF MS that the processes involved can be visualized in a straightforward way that is particularly convenient for working with undergraduate students. In short, laser light is used to excite matrix, which are small but highly conjugated organic molecules (see Figure 1). As these matrix molecules are desorbed from the plate, they become ionized. Analyte molecules (peptides, polymers, small molecules and proteins) associated with the matrix are also desorbed and ionized. All molecules possess are imparted with roughly the same kinetic energy.

Simplified MALDI-TOF MS schematic / Figure 1



At this juncture, analyte molecules and matrix travel down the flight tube, which is kept under vacuum, to a detector that records the time travelled. Because the velocity is related to the mass of the molecules and the square of the velocity, there is an inverse relationship between the mass of the particle and the time it takes to reach the detector. The time-of-flight software interprets the time data and relates this to each particle's mass.



Student benefits

Students benefit greatly from visualizing this process. Indeed, teaching students how to visualize the behavior of molecules is time-intensive and students often stop practicing the moment they finish with a course. This intensive MALDI-TOF learning environment provides fertile ground for teaching students how to imagine the movement of molecules off of the sample plate, into the flight tube and to the detector. Being able to describe the relationship of kinetic energy to mass and velocity is a concrete example of the relevance of physics and math skills to research activities.

There are many additional opportunities to review physics, chemistry and math with students, creating an enduring dialogue between students and faculty that supports creation of a community of science professionals who speak the same professional language, and reinforces the concept of lifelong learning which extends beyond the parameters of a mere course or program of study into a framework that reflects world improvement.

References and notes

1. [Antony Davies](#) and [James R. Harrigan](#), "Why the Education Bubble Will be Worse Than the Housing Bubble," June 12, 2012, www.usnews.com/opinion/blogs/economic-intelligence/2012/06/12/the-government-shouldnt-subsidize-higher-education.
2. Katy Hopkins, "New Three-Year Degree Programs Trim College Costs," Feb. 2, 2012, www.usnews.com/education/best-colleges/paying-for-college/articles/2012/02/29/new-three-year-degree-programs-trim-college-costs.
3. National Research Council, *Bio2010: Transforming Undergraduate Education for Future Research Biologists*, National Academy Press, 2003.
4. Koichi Tanaka, Hiroaki Waki, Yutaka Ido, Satoshi Akita, Yoshikazu Yoshida, Tamio Yoshida and T. Matsuo, "Protein and Polymer Analyses Up to m/z 100 000 by Laser Ionization Time-of-Flight Mass Spectrometry," *Rapid Communications in Mass Spectrometry*, August 1988, Vol. 2, No. 20, pp. 151-153.



5. Franz Hillenkamp and Michael Karas, "Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry of Biopolymers," *Analytical Chemistry*, 1991, Vol. 3, No. 24, pp. 1,193A-1,203A.
6. Timothy J. Cornish and Robert J. Cotter, "Tandem Time-of-Flight Mass Spectrometer," *Analytical Chemistry*, 1993, Vol. 65, pp. 1043-1047.

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