IMPACT
RESEARCH AT THE UNIVERSITY OF MARYLAND

CATHERINE FENSELAU

Techniques to Detect Pathogens

Catherine Fenselau, a professor of chemistry and biochemistry at the University of Maryland, first put whole bacteria in a mass spectrometer in 1975, showing that it's possible to identify microbes without time-consuming steps like culturing or purification. As mass spectrometers have become more sophisticated, so has Fenselau's level of analysis. Her goal now is to build systems that can continuously monitor surroundings for pathogens and toxins.

"We have mostly been interested in agents in the air, such as you might find in a battlefield, the subway or public buildings," Fenselau says. To be practical, monitoring systems must be free-standing and automated. In a place like a battlefield, monitors must also be portable.

CATHERINE FENSELAU

Detection of Pathogens

With funding from the Defense Advanced Research Projects Agency, through two decades, Fenselau has assembled research teams that bring together labs from around the world. She collaborates extensively with scientists from academia, like those at Johns Hopkins University, as well as researchers in the private sector, including Science and Engineering Services Inc., or SESI, based in Columbia, Md.

The automatic monitors that Fenselau envisions will be used to detect bacteria, viruses and protein toxins. A monitor must first collect particles in the appropriate size range—in this case, particles that could penetrate into the lungs—and then use mass spectrometry to tell exactly what the particles are.

"The great thing is we see whatever is there. Everything has a mass spectrum. We can have a universal monitor that is at the same time very specific," Fenselau says. Mass spectrometers comprise a range of machines that can weigh individual molecules as long as the molecules carry an electronic charge. Conveniently, many mass spectrometers are relatively insensitive to substances like oil and rubber, which often exist as aerosols in an environment like a subway station or a battlefield. Compared to such hydrocarbons, proteins readily acquire a charge.

While Fenselau mostly works to detect airborne pathogens, she has also applied her method to liquids. In collaboration with scientists from the U.S. Department of Agriculture, her group developed a way to detect the bacterium that causes anthrax in milk. Identifying pathogens in a matrix like milk is much more challenging than identifying them in air, because many other biochemicals are present.

In collaboration with researchers at the Johns Hopkins Applied Physics Lab, Fenselau and her University of Maryland research team have fielded a system that collects air samples on tape that steadily bring samples from the air into a mass spectrometer. Samples can then be bombarded with laser light to launch molecules into the gas phase and ionize them. Timed tape samples can be stored for reanalysis in the future. All this must happen quickly—in a "detect to protect time frame," Fenselau says.

One of the limitations of putting whole microbes into a mass spectrometer is that the machine will detect only a small portion of the proteins present in the cells. Controlling which proteins are the ones detected is difficult. The ultimate result is a rather basic fingerprint, which can vary depending on the conditions at which a specimen is collected.

To obtain more specific and definite information, Fenselau's group has started to use mass spectrometry to obtain amino acid sequence information from microbial protein fragments. The order of the amino acid building blocks can then be compared to those available in public databases. Nathan Edwards, an assistant research scientist in the University of Maryland's Center for Bioinformatics and Computational Biology, has collected protein information about microbes in an Internet database based on genome sequence data. The database includes sequence information for more than 200 bacteria and viruses and is updated as new species and strains are sequenced around the world. The sequence of just five to eight amino acids from a single protein is usually sufficient to identify a microorganism.

Using proteomic strategies to identify bacteria is one of Fenselau's major innovations in the use of mass spectrometry. Besides this innovation and her first bold decision to put whole bacteria into mass spectrometers, she has also led major advances in how samples are prepared for mass spectrometry. "We've introduced the use of microwave technology for sample preparation," she notes. Conventionally, a digestive enzyme like trypsin is used to break proteins into fragments before they're weighed in a mass spectrometer. Fenselau's research team has shown that microwave and acid treatment also cuts proteins in predictable ways. Compared to digestion with an enzyme, microwave treatment is more compatible with the goal of building a rugged and automated mass spectrometry system. Ultimately, durability and automation are crucial to any device that will identify microbes outside the controlled environment of a laboratory, but instead must operate in public spaces and combat zones. —*Karin Jegalian*

UNIVERSITY OF MARYLAND

Impact Profile is a supplement to *Impact*, a quarterly research digest from the University of Maryland. To learn more about research at Maryland, go to www.umresearch.umd.edu.

Produced by the Office of University Publications for the Vice President for Research, University of Maryland.