MASS SPEC

# The Next Dimension in Protein Analysis

David Clemmer fancies himself a modest guy from a small town who put himself through school playing folk music. Little do his old band buddies from Adams State College in Alamosa, Colo., know that he's also responsible for building a spectacular new mass spectrometry instrument.

The 36-year-old, newly appointed chair of the Indiana University chemistry department has for a few years now been building and perfecting an ion mobility time-of-flight mass spectrometer that has grand possibilities for proteomics. Two years ago his IMS-TOF created a buzz when *Technology Review* named it a top technology for the 21st century. Today, it is under license to the Cambridge, Mass., startup Beyond Genomics, of which Clemmer is a co-founder.

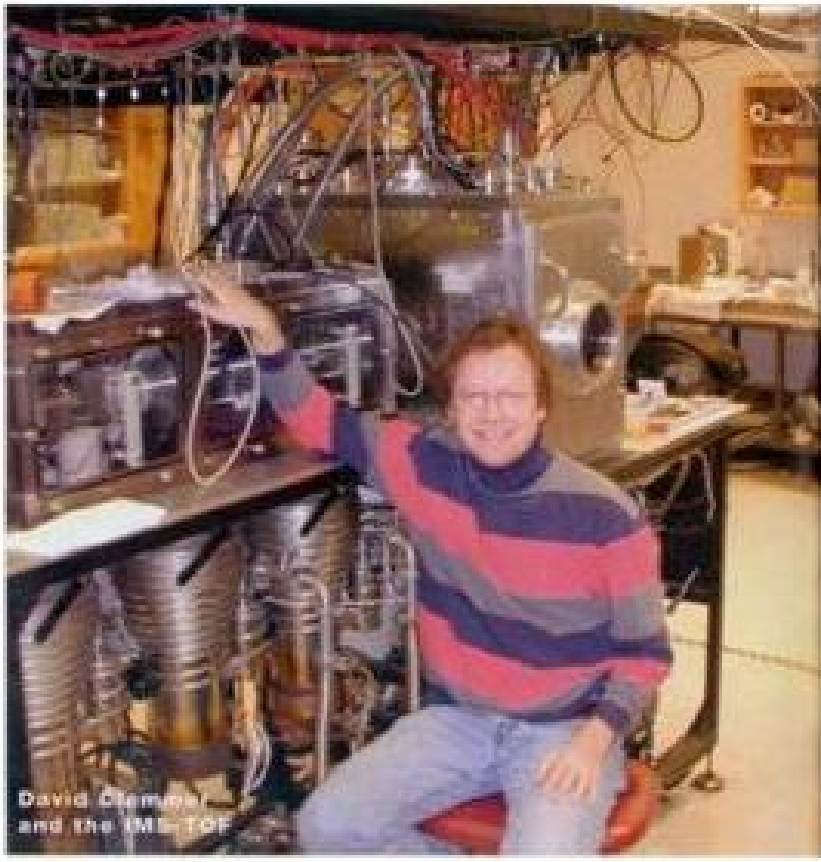
Clemmer's IMS-TOF uses gas as a high-pressure tool to separate ions before introducing them to the mass spectrometer. Crediting precedents set by people such as Herbert Hill at Washington State University, Mike Bowers of University of California, Santa Barbara, and his own postdoc advisor Martin Jarrold of Northwestern University, Clemmer says his contribution to mass spec has been to realize that the separation of gas occurs on millisecond timescales while time-of-flight is on microsecond timescales.

"Because you do things so quickly on millisecond timescales, you can essentially connect any other separation technique to this and then do a multidimensional experiment," he explains.

That's especially helpful for analysis of things as complex as proteomes. "If you have a very complicated sample where you have many species that have nearly identical masses, the mass spectrum will begin to become very complicated and you'll lose peaks underneath other peaks," says Clemmer. "If you can do another separation that's a little bit different in the gas phase before you go into the mass spectrometer, you can see those peaks."

Clemmer says it's easiest to think of IMS-TOF as a "dispersive technology rather than as a filtering technology." Ions aren't thrown away; they're moved apart in time, broken apart, and moved into the mass spectrum. "Those ions that you see fragments from at the same time in the high-pressure separation can be correlated. There's a correlation in time and that can be used to sequence or to gain fragmentation information for ions in parallel. You can't do that with mass spectrometry alone," he notes.

Who better to capitalize on the next big thing in mass spec than Noubar Afeyan, founder of PerSeptive Biosystems? Afeyan flew Clemmer to Boston and pitched him on a business plan that featured his invention as one in a stable of "horizon *technologies*."



David Clemmer and the IMS-TOF

"When I saw how they placed our platform into others I became really excited," Clemmer says. "The idea that we'd be incorporating them into a systems biology platform to study disease states and healthy states sounded really exciting to me, and they had all the right people in place to do it."

Clemmer's first prototype, as well as his first PhD student Steve Valentine, are now installed at Beyond Genomics. While the prototype, which takes up the space of a small office, is set up to perform three-dimensional analysis — liquid chromatography, ion mobility, and time-of-flight — a second-generation machine that Clemmer is still tinkering with will include a fourth dimension: collision. "That's where you get the fragmentation information that helps with the sequencing," he explains.

Beyond Genomics CSO Steven Naylor says, "Clemmer's instrument is going to give us a dimension of resolving capability that is anywhere from a hundred to a thousand times better than just doing conventional online chromatography. It's in effect a second-generation proteomic analyzer."

—*Adrienne Burke*