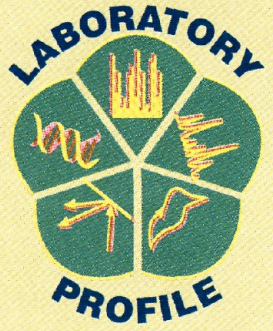



## Making cutting-edge technology work for day-to-day use

When the basis of your business is at the cutting edge of science and technology, creating products and methods that harness this new technology to satisfy customers that are regulated, conservative, and quality-assurance-oriented is quite a challenge. Peter T. Kissinger of Bioanalytical Systems (BAS) has built his business by taking the fruits of biology-based analytical chemistry research and turning them into useful products and procedures for the pharmaceutical and clinical industries.

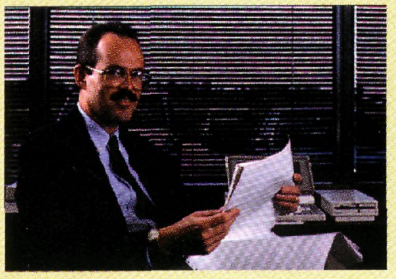
Kissinger began trying to determine small organic molecules in biological materials in the early 1970s. At that time, samples were typically homogenized in acid, a process that not only precipitated interfering proteins but also destroyed the spatial resolution of the sample. He tried to take measurements using electrodes implanted in living tissue, but this procedure was generally unacceptable at that time because of the need to monitor several substances simultaneously. Work is actively continuing on such in vivo electrode biosensors, however.

BAS was founded in the fall of 1974 when Kissinger was on the faculty at Michigan State University. "I pretty much worked all the time and needed a hobby. Building instruments became a way to focus my excess energy. I tried to interest existing companies in our ideas for free—we didn't bother with patents—but they had ideas of their own and technology transfer was not the fad it is now. The primary motive was to have fun. It still is!"

In 1984, Kissinger began sampling in vivo and using dialysis membranes to exclude proteins from samples. "This change of direction," he says, "was inspired by Urban Ungerstedt of the Karolinska Institute in Sweden, a pioneer in this field with whom we began a collaboration. Lee Phebus of Eli Lilly and Jay Justice of Emory University were also a great influence in getting us started with this approach. Because all the early work was done with brain tissue, that's where the method is most highly developed." This simple idea had significant analytical consequences: The samples are free of proteins, there is no need to homogenize tissue or add acid to denature enzymes, and the samples are clean and very compatible with LC, capillary electrophoresis, and immunoassay.

To improve the reliability of microdialysis, Kissinger's company is working with Sue and Craig Lunte of the University of Kansas to explore hollow fiber dialysis and ultrafiltration sampling devices for both in vitro (enzymes, microsomes, cell cultures, and tissue slices) drug discovery work and in vivo pharmacokinetics and toxicokinetics. Kissinger says, "The challenge is to understand the details and to make the in vivo sampling process easy to use. When your focus is on developing instruments and methods, you tolerate a lot. You fiddle, adjust, and make it work long enough to submit a paper or a patent. Then you take it apart and redo it. When your interest is in obtaining quality data, you tend to be a lot more focused on validation, reliability, and convenience issues. QA makes you more conservative.

"We are interested in supporting drug discovery research and clinical trials with innovative analytical chemistry that can be trusted. I've gradually



acquired an appreciation for people who use and regulate analytical chemistry. I've likewise seen how hard it is to take the innovative cutting-edge methodology and make it really work for those who need it day in and day out. We are dealing with a highly regulated and conservative audience [the pharmaceutical industry] that is in a hurry and doesn't have a lot of time to explore new techniques unless the benefits are clearly drawn out. As a commercial entity, we need to clarify these benefits. It's what we have to sell."

Kissinger also enjoys his time in the classroom. "It was a real pleasure working at Purdue and developing BAS for fun. Now it's a pleasure working at BAS and keeping a hand in at Purdue for fun. Although I had a number of truly exceptional graduate students who could work independently, I eventually had to stop taking students a few years ago because I couldn't give them 'quality time,' and it just wasn't fair to them. My arrangement with Purdue worked because of their fabulous analytical faculty, very supportive department heads, and an enthusiastic university administration. I'm not sure that combination exists at too many other institutions.

"The most satisfying thing for me is to read the papers of scientists who use our equipment and cite our papers. Our work has had an enormous impact on neuroscience research for over 20 years. Our assays have been used to develop some of the most successful drugs in history. I think that's pretty neat!"