A Boom for Supercritical Fluids

High performance liquid chromatography (HPLC) with supercritical fluids has many advantages over conventional HPLC and gas chromatography (GC). It is better than GC for thermally labile materials and those that are nonvolatile. Separations of high molecular weight materials are usually faster than can be achieved with HPLC and the resolution is higher (*Science*, 9 April 1982, p. 159). In the past, however, investigators have had to construct their own instruments for supercritical fluid chromatography. This year, Hewlett-Packard Company has introduced a module that will convert its 1082A liquid chromatograph for use of supercritical fluids.

The most important features of the module include: introduction of a flow restrictor downstream from the detector to maintain pressure; a new detector cell that will withstand the high pressures involved and that is cooled to 38°C so that detection is performed at constant temperature and pressure; use of a dual pumping system so that gradients can be produced; and cooling of the pumphead for more efficient pumping of liquid carbon dioxide. The supercritical fluid module costs $8300—slightly more for older chromatographs. The 1082A itself costs $27,700.

Some new uses of supercritical fluids were reported by Richard D. Smith of the Batelle Pacific Northwest Laboratory. He has found that supercritical fluids are excellent media for extracting various plant materials, fulvic and humic acids, and coal. Supercritical ammonia, for example, extracts 25 percent of the humic acid in decayed plant material, whereas other solvents extract only about 1 percent.

Smith and colleagues at Batelle and Brigham Young University have also developed a special interface so that the supercritical fluid HPLC can be attached to a mass spectrometer (MS). The high volatility of the supercritical fluids provides a significant advantage in designing such an interface, he says: the formation of molecular clusters is avoided, as is the persistence of a jet of frozen liquid droplets extending 2 to 5 centimeters into the vacuum region. The result is that the mass spectra show no evidence of clusters. This interface to the MS was used to monitor the extractions by supercritical fluids.

One unexpected advantage of this work was the recognition that supercritical fluids enhance the volatilization of complex molecules. Smith finds that "any material soluble in the supercritical fluid phase is efficiently transferred to the gas phase," where it can be ionized by conventional techniques. They have developed an adaptor so that the supercritical fluid interface can be used for such volatilization directly. They have used this technique to analyze, among other things, the fungal toxins T-2 and diacetoxyscripenol, which are difficult to assay by other techniques.—**T.H.M.**

Microfabrication Is Not Only for Electronics

The wondrous benefits that miniaturization have brought to the world of microelectronics are well enough appreciated. Less well known is that some of the same or similar techniques can be applied to the fabrication of analytical instruments or to parts of them. At least one manufacturer, MMR Technologies, Inc., of Mountain View, California, was on hand at the Pittsburgh Conference to exhibit a miniaturized Joule-Thomson gas expansion cryocooler that could refrigerate small samples to temperatures almost as low as that of liquid nitrogen (77 K).

In a talk at one of the Pittsburgh Conference sessions on new instrument concepts, Tomas Hirschfeld of the Lawrence Livermore National Laboratory discussed some of the concepts involved in making analytical instruments having features with dimensions in the range of 100 micrometers to 100 angstroms, as compared to minimum feature sizes from 1 centimeter to 1 millimeter now. Miniaturization is not simply a matter of making an existing instrument proportionately smaller in every aspect, Hirschfeld emphasized. Gravity becomes less important for very small structures, whereas adhesive forces due to normally neglectable attractive van der Waals interactions can be influential. Similarly, viscosity becomes an overwhelming effect.

Hirschfeld listed several advantages of miniaturization. A lower weight and smaller volume could lead to new applications. A thumb-sized mini–Fourier transform infrared spectrophotometer flew on one of the Surveyor space missions, for example. Miniaturization also brings improvements in speed, uniformity, and ruggedness, as well as lower electrical power consumption.

Researchers at Livermore have built a number of miniaturized devices, which Hirschfeld briefly described. One was a permanent drier that removed water from its environment. Another was a microthermometer that recorded its temperature history. And a third was a microsampler to collect material for a Fourier transform infrared spectrophotometer. These and other microdevices were developed in connection with Livermore's nuclear weapons program, so Hirschfeld could not say exactly how they were used.

MMR Technologies is a 3-year-old company exhibiting for the first time at the Pittsburgh Conference. Its Joule-Thomson miniature cryocooler is the outgrowth of research begun by William Little at Stanford University, who wanted a reliable and convenient cold station for experiments.

Rather than using liquid nitrogen to reach 77 K or liquid helium to reach 4.2 K, cooling by the Joule-Thomson effect requires only gases. Gas at a high pressure that expands through a capillary is cooled, although not dramatically. The effect is enhanced when the cooled gas passes through a heat exchanger that precools incoming high-pressure gas. This cycle continues until the gas either liquifies or reaches a temperature near that of the liquid. The final temperature is set by a balance between the cooling power of the gas and the heat load of the sample.

The microminiaturized part of MMR's cryocooler is the heat exchanger, which is etched into a glass substrate and whose channels are less than 2 micrometers wide. The entire refrigerator assembly fits in the palm of one's hand. Several standard and customized models are available, each of which can cool samples to 80 K for more than 50 hours with only a standard cylinder of dry, commercial grade nitrogen and a small vacuum pump. Future systems will reach to 4

K. Also planned are hermetically sealed systems that do not need to be pumped continuously, and closed cycle systems that reuse the gas.

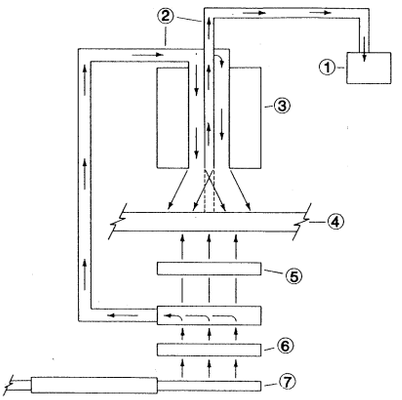
The most expensive standard cryocooler with windows for optical transmission experiments, a temperature controller, and a thermometer lists at $3745.—**A.L.R.**

Optical Fibers Make It into Instruments

Optical fibers provide a useful way to transmit light to a monochromator so that the sample cell does not have to be inside the spectrometer (*Science*, 26 Nov. 1982, p. 875). Two new instruments displayed at the Pittsburgh Conference incorporate fiber optics, and various components to produce fiber optic spectrometers and optrodes—the optical equivalent of an electrode—were also exhibited.

The Kontes Model 800 Scanning Densitometer for analyzing thin-layer chromatograms and other two-dimensional arrays uses a fiber optic system to transmit light to the chromatogram and to carry transmitted or reflected light to the monochromator. Optical misalignments are virtually impossible because of the fiber optics, says the company, and delicate adjustments of the optical system are eliminated. It is therefore simple to set up and use the instrument. The use of fibers with differing admittance angles also reduces interference by reflections from the plate. The instrument costs $7250.

The Focus 2000 system marketed by J & W Scientific Instruments Inc., uses fiber optic cables to carry light to a flow-through detection cell for a liquid chromatograph. By combining fiber optic cables and optical waveguides, it is possible, the company says, to construct almost any type of microvolume flow cell with any desired path length. The Focus (Fiber Optic Computerized Universal Spectrometry) system contains a "powerful integral computer [so that] the commonly used but normally incompatible techniques of absorbance, fluorescence, refractive index, and scattering may be performed simultaneously or serially" on a single sample. The instrument costs $24,750 with a deuterium light source. Optional plug-in modules provide tungsten/halogen, xenon arc, and helium-neon laser sources.



A fiber optic densitometer

The optical system of the Kontes Model 800 Scanning Densitometer. Key: 1, detector; 2, fiber optic light guides 3, scan head (only one of two shown); 4, thin-layer chromatography plate or other media; 5, cover to block transmission for reflectance spectrometry; 6, interchangeable phosphor coated disks convert ultraviolet lamp output to selected wavelengths; and 7, ultraviolet lamp.

A complete line of fiber optic cables, light sources, detectors, optrodes, and accessories to produce specialized optrodes was exhibited by Oriel Corporation of Stamford, Connecticut. The company will also custom-build fiber optic spectrometers to the user's specifications. Fiber optic cables and bundles were also displayed by the Maxlight Fiber Optic Division of Raychem Corporation of Arizona, headquartered in Phoenix.—**T.H.M.**

Artificial Intelligence Comes to Atlantic City

One of the hottest areas in artificial intelligence research is that of knowledge-based or expert computer programs. Stored in the computer is the accumulated wisdom of the "experts" in a certain field. The program can use this information to make deductions concerning data entered into the computer. The best known of these are medical diagnosis programs. A patient's symptoms are entered, and the program "asks" a series of increasingly specific questions whose answers enable the program to conclude the most likely cause of the patient's distress.

Molecular Design Ltd. of Hayward, California, has used this strategy in its database management system for molecular structures and chemical reactions. One program called MACCS for molecular access system allows the user to store and retrieve molecular structure information. One way to access the stored information is to draw on a special graphics tablet a sketch of a molecule or a part of one. The program contains information about the rules of molecular structure and can "clean up" the sketch, after which it searches the database for the molecule or for all larger molecules of which it is a part. A similar capability resides in a program named REACCS for reaction access system. Reactions encountered in the laboratory or in the literature make up the database. One of the search capabilities is to find all the reactions in the database that contain a specific molecular substructure graphically entered on the graphics tablet.

GENOA is a program that finds all the molecular structures allowed for a particular molecular formula entered by the operator that are consistent with certain constraints, also entered by the operator. The structural candidates are displayed on a video screen and may be entered into the MACCS database. GENOA is an elaboration of an expert program named DENDRAL that was written by artificial intelligence researchers at Stanford University to deduce molecular structures from mass spectrometry data. DENDRAL's knowledge base consisted of rules for deriving constraints on molecular structure from experimental data, a procedure for generating candidate structures that satisfied the constraints, and rules for predicting mass spectrograms from the proposed structures.

A fourth program, ADAPT, allows the determination of structure-activity relationships by the use of pattern recognition and other statistical techniques. In one study at Pennsylvania State University on the carcinogenicity of nitrosamines, researchers using ADAPT were able to find 22 structural descriptors that provided the ability to determine which molecules were and which were not carcinogenic.

The Molecular Data programs are designed to run on "mid-sized" machines with the considerable computing power needed for their execution. Prices range from $100,000 to $150,000 subject to the specific needs of the purchaser.—**A.L.R.**