A Separation Technique with Potential

Electromolecular propulsion has been scoffed at and scorned, but its persistent inventor may finally be nearing a payoff

"If Norman Haber did not exist, Ronald Reagan would have to invent him. . . . He is the kind of scientist, I suspect, that Ronald Reagan is looking for wherever he can find one," says L. Pearce Williams, a historian of science at Cornell University who specializes in electrochemistry and maverick scientists. "Norman Haber does not have a Ph.D. Norman Haber is not associated with an academic institution or with a research foundation. Norman Haber has never had an NSF grant."

But Norman Haber has a dream, one that he has pursued through 15 years of frustration and discouragement. The dream is of a new way to separate materials ranging from rare earths to biological macromolecules through a process he calls electromolecular propulsion or EMP. He has persisted through outright scorn from some of his peers, and indifference from most, to the point where he now has two patents on the process, a recent publication in the *Proceedings of the National Academy of Sciences* [**79**, 272 (1982)], and two joint ventures that are exploiting potential commercial applications of EMP. After 15 years of battle, Haber remains somewhat defensive about an uncompleted education and his inability to explain EMP theoretically, but hopeful that he is finally on the verge of vindication.

Haber was a graduate student attending New York University at night when he dropped out in 1967 short of his degree. "I looked around me at people spending 10 years getting their Ph.D.'s while their families lived in virtual poverty and I decided that wasn't for me," he recalls. Two papers on electrophoresis published with Irma Tuck-Weiss were his sole contribution to the scientific literature.

The idea for EMP had been in his head for some time, and he began experimenting in his basement laboratory on Manhattan's upper West Side, supporting his research and his family by designing, building, and selling special electromechanical devices, including motor controls, remote controls, and dialysis equipment. By 1969, he had constructed a console-sized device "that clearly showed that EMP would work the way I thought it would."

To understand EMP, it is probably necessary to be familiar with electrophoresis, a technique developed in the early 1930's by the Swedish chemist Arne Tiselius, who was subsequently awarded a Nobel for his work. For example, mixtures of electrically charged molecules are placed in a flat aqueous gel or on saturated filter paper and an electric potential, typically 1 to 20 volts per centimeter (V/cm), is applied. The molecules migrate in the field at speeds characteristic of their total charge, mass, and cross-sectional area, and can thereby be separated from one another.

The rate of migration can be increased by increasing the voltage. The increased speeds are accompanied, however, by increased temperatures resulting from the large current flow. These temperatures disrupt separations and can destroy the gel. Practical considerations thus demand that most electrophoretic separations be conducted at low voltages over relatively long periods, typically hours. Some new electrophoresis systems can operate at potentials as high as 50 to 100 V/cm, but only with special cooling equipment.

High voltages give rapid separations if the medium has very low conductivity.

Haber's key concept was that much higher voltages could be used to give rapid separations without heat buildup if the medium had very low conductivity—a possibility foreseen by Tiselius but apparently never explored. By using nonpolar solvents boiling above 140°C, Haber was able to operate at potentials of 1,000 to 25,000 V/cm with currents ranging from less than 1 microampere to 10 milliamperes. In contrast, conventional electrophoresis has currents of 50 to 100 milliamperes.

A nonconductive medium, alone, is not sufficient for EMP. Operation also requires the addition of small quantities of modifying agents—typically, strong electron donors and acceptors—to adjust conductivity. Haber likes to draw an analogy between this process and the use of dopants to modify the conductivity of silicon in transistors. Some examples of modifiers that can change the migration rates of nonpolar substrates include tetrahydroionone, 4,5-dimethylisooxazole, *N*-methylacetamide, sulfolane, and tetrahydrofurfuryl alcohol.

The precise mechanism by which these materials affect conductivity in the systems is still a mystery, but Haber claims that there are subtle charge transfer effects between the modifiers and the substances to be separated. There is a rapid interchange of electrons between the participants in such a complex; there is a very brief period between the time that an electron is transferred from one member of a complex to the other and the time that an electron is returned. During this brief period, the molecule has a positive charge. Haber argues that the selection of an appropriate combination of solvents and modifiers can prolong the period between transfers so that the molecules migrate, even though they have no formal charge or polarity. He calls this "chemoelectric" mobilization.

Whatever the mechanism, EMP differs from the classical electrokinetic process in that it is nonlinear, nonelectrolytic, and nonelectrostatic. In an electrolytic system, charge is carried by ions, while in an electrostatic system, charge is carried by electrons. EMP, says Haber, "doesn't follow either completely, but exhibits a character of its own. Molecules behave unexpectedly and show very high migration rates—orders of magnitude greater than can be achieved electrophoretically." It is nonlinear in that internal resistance, effective current, and the mobilization rates of the molecules do not vary directly with the applied voltage. One effect of this nonlinearity is the observation of "threshold currents" below which specific molecules will not migrate. It is thus possible to effect separations not only through differences in migration rate at constant voltages, but also by increasing the voltage slowly so that threshold values for each component of a mixture are exceeded sequentially.

The net effect of these characteristics is that separations can be performed rapidly, in seconds as opposed to hours, and over very short distances. The short time drastically limits diffusion of the

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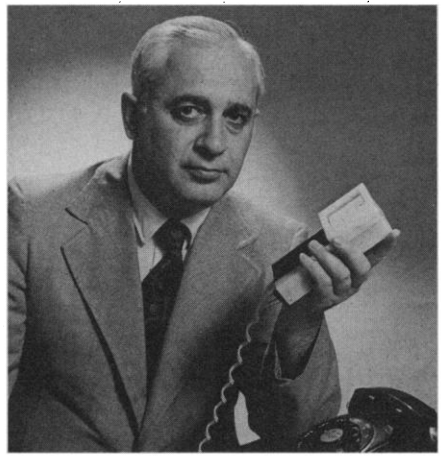
substrate in the solvent, making separations much cleaner. In a recent public demonstration conducted by Haber, dyes moved visibly, and a clean separation was obtained in little more than a second. When the polarity of the electrodes was reversed, the spots returned to their original starting points with virtually no blurring, indicating the absence of diffusional effects.

Most separations require a specific mixture of solvents and modifiers. One example cited in the paper is a medium designed for effecting migration of aromatic hydrocarbons. It consists of 33.3 percent 1-butoxyethoxy-2-propanol, 12.5 percent bis(2-methoxyethyl) ether, 31.2 percent ethylene and propylene carbonates (85:15, by mixed volume), 14.5 percent Carbitol acetate, 6.5 percent γ-butyrolactone, and 2 percent dimethylmorpholine. The migration of many aromatic hydrocarbons in this medium on Whatman number 4 filter paper was about 2 centimeters per minute at 1000 V/cm. Other substances that can be separated in other media include metal salts, organometallic compounds and complexes, and a wide variety of organic species of moderate and high molecular weight. Separation quantities can vary from micrograms for analytical procedures to grams for preparative applications.

In 1973, Haber constructed a pocket-sized instrument and filed a sweeping patent application for high-voltage EMP technology. The Patent Office resisted his claims, arguing that the device was simply a refinement of electrophoresis—a view still held by some investigators. After an exhaustive review of Haber's work and the convening of a panel of experts to assess the invention, the Patent Office issued the patent (No. 3,984,298) in 1976. A second patent covering low-voltage applications, among other things, was issued in 1979 (No. 4,146,454). The process has also been patented in Canada, Europe, and South America. (Publication in the *Proceedings* also took about 4 years as Haber was faced with similar objections from referees.)

Haber has taken what might be considered a rather unorthodox approach in promoting the technique. Most of the details were kept secret while the patent application was pending; the recent paper was the first substantial disclosure of precise operating conditions. He has not made the device available to other investigators. "We tried that once, but it didn't work out. We found that it takes several months of work with me, or with my group, to get the practitioners sufficiently familiar with the technique for them to use it. We also haven't sold any of these devices. My basic interest now is to develop protocols for their use and, if we are ever to sell the instruments, my inclination would be initially to sell the package of software with the hardware, rather than expect a researcher to stop his work and take the time to develop protocols himself." He concedes, however, that the patent application and the paper contain enough information for a competent investigator to construct his own apparatus, and it may well be that the technique will not gain acceptance until one or more investigators do so.



Maverick scientist?

Norman Haber holds a portable cell used for EMP separations.

Meanwhile, his company (Haber, Inc., of Towaco, New Jersey) has a half-dozen postdoctoral fellows developing selected applications and looking for others. A good example of the former is a joint project with Victor Gurewich and his colleagues at the Vascular Laboratory of St. Elizabeth's Hospital in Boston. Gurewich's group has found that the relative concentrations of high-density lipoproteins in blood serum can be used to predict susceptibility to heart disease. They have developed a sophisticated electrophoretic assay for measuring this distribution, Gurewich says, "but it requires a Ph.D. to run it, and he can only do 12 samples a day." Haber has demonstrated that some lipoprotein analyses can be performed by EMP in about 1 minute. The two groups have formed a joint venture called Life Signs Research Associates to refine and standardize the assay so that it can be used at St. Elizabeth's and other hospitals.

EMP is particularly good for isolating valuable metals, says Haber. Last November, Haber, Inc., signed an agreement with Houston Mining & Resources, Inc., to form another joint venture that will build a pilot plant to demonstrate the use of EMP to recover gold from low-quality ore. Houston Mining has estimated reserves of gold exceeding 6 million ounces in its "Black Hawk-Silver Reef" mine near Victorville, California, but the metal is intimately associated with an active form of carbon, which makes conventional recovery processes uneconomic. Laboratory tests suggest that the gold can be separated from carbon by EMP. Haber has a similar silver-recovery process for which he hopes to have a pilot plant in operation within a year. The details of both processes are proprietary, but they involve hydrochemical dissolution of the ore and chemoelectric separation of the ions. The company is also "about two-thirds of the way through scale-up" of a process for separating gram quantities of rare earths.

Independent assessment of the validity of Haber's claims is particularly hard to obtain at this point. Most of the people who are intimately familiar with the process are investors in the company. Rollin D. Hotchkiss of The Rockefeller University, who sponsored the paper in the *Proceedings*, says that the phenomenon demonstrated by Haber "surprises everyone who sees it." He felt that there is "enough possibility that it is a new phenomenon" and "enough interest in the unusual effects" that the paper should be published. He concedes, however, that "there are enough doubts about the underlying theory that many people have washed their hands" of the topic. Similar views were expressed by John Cann of the University of Colorado Medical School, who calls EMP "an unexplored method that has promise."

A more critical view was espoused by Leonard Ornstein of Technicon Corporation, who is widely acknowledged to be one of the major figures in electrophoresis. Ornstein says that Haber has made "interesting observations" of "phenomena that people have ignored to the detriment of science." He thinks the publication will have a positive effect because it "ought to stimulate some people . . . to look at it a second time." Nonetheless, he argues that Haber has "generated a theoretical house of cards that is unjustified." Simply put, Haber's "explanation is not tenable" and "does not do justice to the phenomena." Ornstein considers EMP to be a variant of electrochromatography, which differs from electrophoresis only in that there is an electrostatic interaction between the substrate and the solvent. In conclusion, he says, "I'm very positive about the phenomenon, and very disappointed about the attention that was given to mechanism."

—THOMAS H. MAUGH II