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Ion Selective Electrodes

Their Development and Commercialization Part 1

by Truman S. Light (Consultant) and Martin S. Frant (Orion Research, Inc.)

The paper presented here is a summary of the talk given at the September 18, 1997 meeting of the Northeastern Section at Keene (NH) State College and a condensation of two symposium papers: (a) Frant, M.S. "Where Did Ion Selective Electrodes Come From?, The Story of Their Development and Commercialization", *J. Chem. Ed.*, **1997**, *74*, 159-166; (b) Light, T.S. "Industrial Use and Applications of Ion Selective Electrodes", *J. Chem. Ed.*, **1997**, *74*, 171-177; given at the seventh Waters Symposium, March 1996.

The Founding of Orion Research

We begin by looking at the formation and history of Orion Research. In 1961, John Riseman was a 27-year old electrical engineer who, unhappy at working for others, had started a consulting business in the medical instrumentation field, operating out of his home. Using the newest transistors which had just become available, he developed a dual-input pH meter. From his consulting experience he concluded that, to sell his meter to some company, he needed sodium and potassium electrodes to go with it.

For sodium, he searched the literature and came upon the work of George Eisenman, a medical researcher at the Pennsylvania Neuropsychiatry Institute, who had been studying the transmission of cations through cell membranes and tried to make sodium and potassium electrodes for this work. In 1957, he published the results of his group's investigation into the effect of glass composition on selectivity for sodium and potassium ions. They had come up with what is today still the best glass composition for sodium, designated as NAS 11-18.

Riseman hired Eisenman as a consultant to what was now called "Riseman Development Laboratories". Riseman knew very little chemistry, and went to the MIT Industrial Liaison Program for help in developing electrodes. They referred him to an electrochemist, Assistant Professor Dr. James W. Ross. Ross and Eisenman first met in Riseman's kitchen.

Eisenman's NAS 11-18 sodium glass was high in alumina and was extremely high-melting, not something that could be made in Riseman's kitchen. So they turned to the Corning Glass Work's Research department for help in preparing test samples.

Corning watched the work that Riseman was doing with considerable interest. (There was another factor that may have influenced Corning's decision: According to legend, at one point in the 1930's, Arnold Beckman had approached Corning to buy his pH patent, so that he could concentrate on his duties at Cal Tech. Corning turned down the offer, apparently deciding that the electrodes used too little glass to make it worthwhile. The story was well known at Corning, and now another opportunity had appeared for getting into a high-value glass-based instrument business.)

Instead of the research contract, a much broader arrangement was negotiated. Riseman and Ross formed Orion Research, a private consulting company. Orion would do research under contract to Corning, and Corning would pay all the bills. Orion would not make a profit from the Corning contract. Instead, Orion would get a royalty from the sales of any new product they developed for Corning. Orion was now ready to

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enter the field of "specific ion electrodes". The company was incorporated in May 1962, and in July Ross left MIT. There was no question of where the new company would be located. Cambridge in the early sixties was an exciting place, and Riseman felt that it had the right kind of atmosphere for a young company. Work began on new glass electrodes.

Orion's beginning investigation of new glass electrode materials was suddenly halted. A business decision by Beckman Instruments had a profound effect on the start-up company: Beckman, since its inception, had been selling pH electrodes and meters through laboratory supply dealers, such as Fisher Scientific or A.H. Thomas. They decided, instead, to sell directly, using their own sales force. This left the distributors without a major source of pH electrodes and meters. Corning management decided, that if they could move quickly enough, this was a golden opportunity to get into this field. The decision was made in July 1962, and Corning turned to Orion to develop the new products.

By January 1963 Ross, working with Norman Hebert at Corning, had developed a new glass composition, making the first "all-purpose" pH glass (before that, glass electrodes had been useful either between pH 1 and 12 or, using a high resistance, special purpose glass, for the range pH 12-14). Orion also developed a new, transistor-based pH meter (Corning Model 12) improving on the technology Riseman had developed earlier. In a little over six months, Corning was in the market with innovative new products.

Orion turned back to the problem of making glass calcium electrodes. Ross soon made the disheartening discovery that glasses reported in the literature were non-conducting. It was here that he made a remarkable leap. "If we can't get the ion to move from the site, why not cut the bonds holding the site, and let the site move, too? " This was the concept of the liquid membrane electrode, the true starting point of the ISE revolution. The advantage of the Ross approach was that it gave a basic and reproducible system in which the selectivity depended on the structure of the water-insoluble "carrier" and the nature of the solvent, and it appeared that the limits of the ability to measure any species depended only on the ingenuity of the organic chemist. Martin Frant joined Orion at this stage, and began to explore the effect of structural changes on Ross's first calcium exchanger and solvent (the calcium salt of dioctyl phenyl phosphoric acid and dioctyl phenyl phosphonate). He had picked these because phosphate and polyphosphate form stable complexes with calcium, but not with sodium or potassium. It was necessary to learn how to assemble and test the many possible combinations of solvent and carrier in order to quickly screen the new ideas that were being generated almost daily.

At this point, Corning's success of competing with Beckman in selling glass pH electrodes had unexpected consequences. Corning's royalty payments to Orion for pH electrodes and meters were becoming substantial and the Corning management, embarrassed, made another effort to buy Orion. For a group used to a totally free-wheeling atmosphere and the cultural milieu of the Boston area, the Corning large-company structure was not a tempting prospect. Instead, Orion agreed to give up the royalties if Corning would forget the "future non-competition" clause in the contract. The two companies separated, and became competitors. There was an understanding that the two companies would meet in five years to discuss cross-licensing of patents developed in the interim. This might be viewed as an experiment, in which a little company, with almost no finances, started from the same technical base as a major corporation. There was no meeting in five years because Corning did not develop any significant patents in the field.

The Foxboro Company

At the point of separating from Corning, Orion had no products and no income. Its directors went to The Foxboro Company, looking for help. Foxboro said they would buy 10% of the company, if Orion could demonstrate their ability to make electrodes by developing a hypochlorite or sulfide electrode. Ross remembered a paper by Kolthoff, and wondered if that approach would work for sulfide, using silver sulfide membranes instead of silver chloride.

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Ion Selective Electrodes II

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The first part appeared in the October issue.

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Two Foxboro managers, John Dobson and Charles V. Cooper influenced the development of analytical instumentations. Truman Light joined The Foxboro Company in 1964. Shortly after Light arrived at Foxboro, Dobson and Cooper came into his lab, saying that they were interested in the products of a company (not otherwise identified) that had invented "Specific Ion Electrodes" which could dip into solution and immediately measure many ions. Would he do a "blind" evaluation and make some test samples to be taken to this company and see how well they did? Light neglected to tell Dobson and Cooper that the research community is composed of scientists with like interests and he had known Jim Ross several years earlier while residing temporarily at MIT. He entered into the spirit of the request and prepared one pure calcium solution, a second with a fair amount of acid in it and another with the nearest relative in the periodic table that he thought would interfere—barium. Orion's electrodes did well in the analysis of the first two solutions and not so well on the third. Later, this electrode was

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brought on to the market as an electrode for divalent cations and has been quite successful as the "water hardness" electrode. Foxboro invested in Orion in 1966. The association between the two companies brought Ross, Frant and Light into close professional contact.

The business arrangement between the two companies permitted their research departments to cooperate and develop new products suited to each of their business goals.

The Foxboro Company developed "on line" chemical analyzers to meet the needs of the process chemical industries. These requirements included unattended chemical analysis in production environments with low instrument maintenance requirements. Methods were developed to monitor such diverse applications as continuous monitoring and control of fluoride addition in public water supplies, salt in tomato juice, sulfide in the "black liquor" of the pulp and paper industry, water hardness in laundries and sodium in ultra-pure water. Procedures were developed for on-line reagent addition, computer correction of interfering ions such as pH, temperature corrections for elevated temperature processes and pressure corrections for the normally disastrous effect of process 'back-up' into reference electrodes.

Beyond Glass

Orion continued its research and development of ion selective electrodes. In addition to the liquid ion exchange membrane electrodes, others were created. A new class of liquid electrodes, developed by Simon, were found for ammonium and potassium ions, using the antibiotic valinomycin. Light resistant silver sulfide "solid state" electrodes were developed for chloride, bromide, iodide, and sulfide ion measurement.

Silver-based membrane materials could never yield a fluoride electrode, because pressed pellets of silver fluoride are soluble. Frant saw an advertisement in Analytical Chemistry offering something new: rare earth single crystal fluorides for use in lasers, and immediately asked for samples. The rest is history. The fluoride electrode rivaled the pH glass electrode in selectivity, sensitivity and freedom from interferences. The electrode replaced a difficult wet analysis, was almost free from interferences, and was strong and durable. Immediate approval came from a giant among analytical chemists, James J. Lingane at Harvard. His paper convinced many skeptics that ISEs were practical devices. The flouride electrode gave Orion an important source of cash flow, and to this date, almost thirty years later, it is still the largest selling ISE with about 300,000 fluoride electrodes sold world-wide by Orion and its competitors.

Growing Pains

At Orion, due to growing pains, typical for a small company, the burst

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of creative activity in new electrodes slowed down considerably. Somehow, one expects that having invented the better mouse trap, all would be well ever after. However, as the number of Orion ISEs increased, so did a stream of papers on methods using them along with a flood of review and popular articles. This created a concern among the traditional instrument manufacturers who feared that they would be left out of a burgeoning new field. Orion tried to expand into all the obvious openings that had been created, but it never had the "deep pockets" of companies such as Corning Glass and Beckman. Adding to this was the burden of patents. These are supposed to reward inventors by giving them a period of exclusive sales, and in the end they do work that way. But in the beginning, they were also a considerable drain on Orion's resources. It was important for Orion to apply for patents as quickly as possible, but the rate at which new inventions were coming in those first critical years meant that financial stress had to be balanced against future protection. U.S. applications were straight forward, but every overseas application required separate filings and translations. As a result, the fluoride electrode was patented in only a limited number of countries. During the time between applying for a patent and its issuance, anyone is legally free to copy the invention and some did. Refereed papers were published as quickly as other work would allow. However, these told how electrodes were made and simplified copying. When the patents began to be issued, some of the major companies were fearful of losing a toehold in an important new business and continued to infringe, knowing of Orion's small size and limited funds; litigation would be costly and slow. One company was persuaded to stop only when it was sued in Switzerland, where a deliberate violation of a patent is a criminal offense.

ISEs were not only chemical devices but they also had important biomedical applications; Foxboro had shown that there was a process control

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market, as well. Each business required its own electrode construction, its own instrumentation, and had its own technology. The inability to commit adequate resources to the biomedical program, as a result of all of these conflicting pressures, was a strong factor in the decision of a group to leave Orion, a story related by C.C. Young of Nova Biomedical Co.

The first Orion pH meter had preceded the sale of the first ISE, and was intended to provide a business which would support the ISE research. The meter business proved to be difficult and expensive since it went head-to-head with the industry giants. Orion could compete only by providing significant innovations, but this meant constantly developing new laboratory instruments as the competitors played catch-up.

The End of the Era

Although a few more important electrodes would be added (cyanide, ammonia, nitrogen oxide, etc.), the "electrode of the month" era could not be sustained, , and Orion became more conventional. Business managers were brought in and the free-wheeling atmosphere ended. Orion, as a start-up, had a corporate culture that vigorously supported wild ideas and experimentation. It had a few bright, creative technical people who worked well and easily with each other. They drew very little from the prior art but developed a good understanding of the mechanisms of ISE's, and mastered the important craft of building and testing them. Such startup corporate settings do not last long - the realities of the business world and business management soon take over. But, they are exciting and fruitful times while they last and, in this case, they left a legacy of a technology that has made life easier for analytical chemists everywhere. ◇