ESSAYS ON APS CLASSIC PAPERS

First electrodes for blood Po2 and Pco2 determination

John W. Severinghaus

Department of Anesthesia and the Cardiovascular Research Institute,
University of California, San Francisco, California 94143


During World War II, trained as a physicist, I worked at the Radiation Laboratory at Massachusetts Institute of Technology on radar, and in 1949 I obtained an MD at Columbia University. In mid-1953, the doctor draft interrupted my physiology postdoctoral work with Julius Comroe (1911–1984) and anesthesia residency with Robert Dripps (1911–1973) at the University of Pennsylvania. In the U.S. Public Health Service, I was assigned to the National Institutes of Health as director of anesthesia research at the newly opened Clinical Center. Cardiac and neurosurgery at that time used hypothermic anesthesia. A new paper claimed that hypothermia blocked pulmonary CO2 excretion. Doubting that work, I developed precise laboratory pH analysis and Van Slyke manometric extraction of plasma total CO2, a tedious way to compute Pco2 by the Henderson-Hasselbalch equation. Using dogs, I proved that publication was wrong, due to failure of the author to correct lab PCO2 values to low body temperatures.

In September 1954, at the Fall Meeting of the American Physiological Society (APS) in Madison, WI, Richard Stow, Ph.D. (1916–), of the Department of Physical Medicine at Ohio State University Medical School (Fig. 1), described his invention of a CO2 electrode (3). He had wrapped a wet rubber glove around his homemade pH glass and internal reference electrode. CO2 diffused through the rubber reduced the pH of the water film. He calibrated its logarithmic response with several gas mixtures of known PCO2. However, it drifted, and he was skeptical of ever making it stable. During the discussion period, I suggested adding bicarbonate to the film of water to stabilize it. He replied that he assumed that bicarbonate would buffer the pH, eliminating the signal. We agreed that I would proceed to test the idea. Stow’s department required him to publish in the Archives of Physical Medicine and Rehabilitation, which initially lost his paper, causing a delay until 1957 (4).

In April 1956, at a Federation of the American Societies for Experimental Biology (FASEB) ad-hoc meeting on methods of blood Po2 analysis, which I had organized, Leland Clark, Ph.D., a biochemist at Antioch College, Ohio, revealed his invention of a self-contained polarographic oxygen electrode relationship between pH, Pco2, and bicarbonate ion concentration in aqueous electrolytes. The optimal HCO3− proved to be similar to that of blood and spinal fluid, 10–25 mM. Freeman Bradley, my laboratory technician, and I constructed a cuvette to hold a small blood (or calibrating gas) sample anaerobically at the surface of the CO2 electrode. We initially believed that a calomel reference electrode would be more stable than chlorided silver (it wasn’t). We tested various spacer materials to hold electrolyte between the pH glass surface and membrane, choosing sheer nylon stocking, despite the refusal of the purchasing department to buy them. We found Teflon membrane more dependable than rubber, although slower (lower permeability to CO2). Initially the cuvette was housed in a water jacket for temperature control at 37°C.

I did not immediately consider publishing or patenting the electrode, since it was Stow’s idea and he had decided not to patent it. He had offered it (in a fateful letter, see below) to Beckman Company before his APS lecture, but they refused.

In April 1956, at a Federation of the American Societies for Experimental Biology (FASEB) ad-hoc meeting on methods of blood Po2 analysis, which I had organized, Leland Clark, Ph.D., a biochemist at Antioch College, Ohio, revealed his invention of a self-contained polarographic oxygen electrode...
On October 4th, 1954, he had built the first model within an hour of experiencing an “AHA!”, a sudden insight. For monitoring oxygenation in his blood bubble oxygenator, he had previously published the design of polarographic electrodes, which he made by sealing a platinum wire with a bead on its tip into a glass tube. He covered the cathode with cellophane (to avoid cathode poisoning by blood protein) and used a reference electrode in the blood. It was useless for analysis, because the very permeable cellophane resulted in a very high cathode oxygen consumption. His AHA! was to realize that he could combine a platinum cathode with a chlorided silver reference wire in a self-contained electrode. This made possible the use of an electrically nonconducting and much less permeable polyethylene membrane over the tip. Before his disclosure at FASEB, Clark had arranged for the manufacture of the electrode by the Yellow Springs Instrument Company. I obtained one within a few weeks.

I found that the YSIC-Clark electrode signal was at least 25% lower in water or blood than in a gas of equal \( P_O_2 \). Bradley and I therefore constructed a cuvette for the electrode containing a tiny stirring paddle. Even then, Clark’s electrode could not be accurately calibrated with gas but only with blood equilibrated with a known \( P_O_2 \). We built a small thermostated water bath containing both a small blood tonometer and the stirred \( P_O_2 \) cuvette. In 1957, we added our Stow-Severinghaus \( P_CO_2 \) electrode to that thermostat, the first blood gas analysis system (see figures 1 and 2 in Ref. 2).

During the APS Fall Meeting in Iowa City, in 1957, Comroe persuaded Stuart Cullen (1909–1979) to come from Iowa to organize an independent anesthesia department. Comroe, calling from Cullen’s Iowa office, had had to persuade Leon Goldman, chairman of surgery at the University of California, San Francisco, to abandon his control of the anesthesia section. I then agreed to join them in July 1958.

In the fall of 1958, at the University of California, San Francisco, Bradley and I added a MacInnes-Belcher pH electrode to the \( P_O_2-P_CO_2 \) thermostat, making the first three-function blood gas analyzer (Fig. 2).

Clark sold his patent to the Beckman Company, which rewrote it to apply to all membrane-covered electrochemical analyzers (including the prior Stow electrode.) After nearly 15 years of litigation, when the court discovered that Beckman had Stow’s letter (above) when they revised Clark’s patent, Beckman was found guilty of fraud, paid triple damages to a company they had sued, but paid nothing to Clark. Beckman miniaturized the cathode, essentially eliminating the need for stirring of the sample. Forrest Bird, MD, persuaded the National Welding Company of San Francisco (who made his Bird respirators) to market the \( P_CO_2 \) electrode. Several firms began marketing three-function blood gas analyzers in the early 1960s.

In 1966, when blood gas analysis had become widely used clinically in surgery, anesthesia, intensive care, and emergency rooms, a survey of physicians found blood gas analysis the most useful and important laboratory test. My subsequent work involved finding good physiological problems needing my blood gas analyzer solution. In Piet Hein’s grook, Last Things First, the inventor/poet writes

| Solutions to problems are easy to find  |
| The problem’s a great contribution   |
| What’s truly an art is to wring from your mind |
| A problem to fit a solution.            |

REFERENCES