lethal factors in this case, they performed experiments in 4 rats, 7 rabbits, and 1 dog. These animals were treated with large doses of desoxycorticosterone but with no excess salt, the rats for 87 days, the rabbits for 15–183 days, and the dog for 70 days. The dog received 5 mg of desoxycorticosterone daily by subcutaneous route. The microscopic findings in the dog were as follows: foamy hepatic cells with collections, in the portal area of plasma cells, eosinophiles, polymorphonuclear leucocytes and phagocytes containing brown pigment. Sections of other organs were found to be normal, except for moderate degeneration of the renal tubules. In 3 rabbits the livers disclosed a diffuse sprinkling with eosinophiles, and in the other 2 rather severe fatty changes. The livers of the rats seem to have been normal.

The changes we have observed in dogs resemble more nearly those reported in the human by Forster, *et al.* (*2*) than their findings in the dog and in the rabbits. This may be explained by the fact that their patient received additional salt while their experimental animals did not. In our dog No. 5, which received no additional sodium chloride, pathological findings in the liver were less pronounced. We feel that the periportal fibrosis found in this dog was not caused by the desoxycorticosterone, but that it may have existed before the experiment.

Thus, pathological changes in the liver were found in each of 6 dogs given desoxycorticosterone and sodium chloride. The changes in the livers consisted of focal and diffuse necrosis (essentially central), fatty degeneration, hyperemia, hemorrhage, and accumulation of pigment. One dog that had received desoxycorticosterone and no salt in his drinking water showed fewer pathologic changes, namely, massive hyperemia and marked pigmentation of the liver cells. Control dogs, receiving only peanut oil by injection and sodium chloride to drink, showed some cloudy swelling or no changes in the liver, and untreated dogs showed no pathologic changes in the liver.

It is generally conceded that noninfectious liver necrosis is due to two main factors, nutritional deficiencies or toxic substances. We feel that the effects of desoxycorticosterone on the livers of our dogs were of a toxic nature, and that the toxic effect was enhanced by the additional salt administered. The doses of desoxycorticosterone given to our dogs were relatively large, but the case of Forster, *et al.* demonstrates that overdosage of desoxycorticosterone can happen in the human and can result in severe and fatal consequences.

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The Use of an Electrolytic Injector as a "Compensating Device" in Electrophoresis

P. Johnson and E. M. Shooter

Davy Faraday Research Laboratory,
Royal Institution, 21 Albemarle Street, London, W. 1

Some form of compensation device is usually essential for experiments requiring migration over path distances greater than the actual length of the cell or for attempting electrophoretic separations of proteins. The so-called compensation device is an instrument designed to produce a very small flow of the bulk of the liquid in

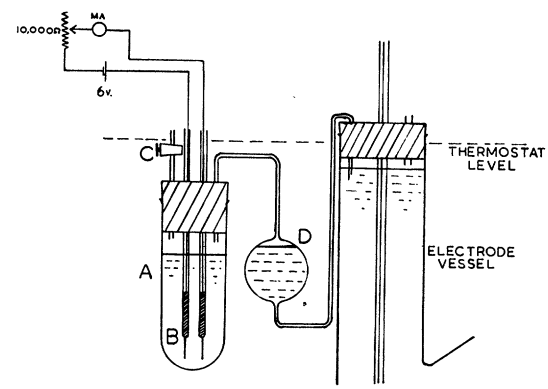

FIG. 1. Diagrammatic form of the electrolytic compensator.

the Tiselius U tube in the opposite direction to the migration of the protein boundary, thus enabling the boundary to be held stationary or even moved in the reverse direction. The design of such a device has followed chiefly two main principles. First, Tiselius (*4*) obtained the displacement of the bulk liquid by slowly dropping a plunger into one of the open electrode vessels of his original apparatus. Longsworth and MacInnes (*2*) later introduced the motor-driven syringe for use with the electrophoresis apparatus which had one closed electrode vessel. A modification of the first principle enabled Svensson (*3*) to use a plunger instrument in the apparatus with both electrode vessels closed. The electrolytic injector to be described here is suited to the original apparatus of Tiselius with both electrode limbs open, or to the modification containing one closed electrode vessel.

The principle of electrolytic injection has been applied in many fields (e.g. *1*) since it was first described, and it remains only to give some indication of one form of the apparatus which may be used for compensation in electrophoresis. The closed vessel, A (Fig. 1), contains approximately $\frac{N}{10}$ H_2SO_4 (or any suitable electrolyte solution) and two platinum electrodes, B (wire of 0.5-mm diameter or foil), sealed in glass tubing to provide external mercury cup contacts. A capillary tap, C,

enables the nozzle and bulb, D, of the injector to be filled with the buffer being used in the particular experiment. The whole may be conveniently fitted to the stand supporting the Tiselius cell and can therefore, apart from the arm entering the actual electrode vessel, be completely thermostatted. In this model, buffer solution

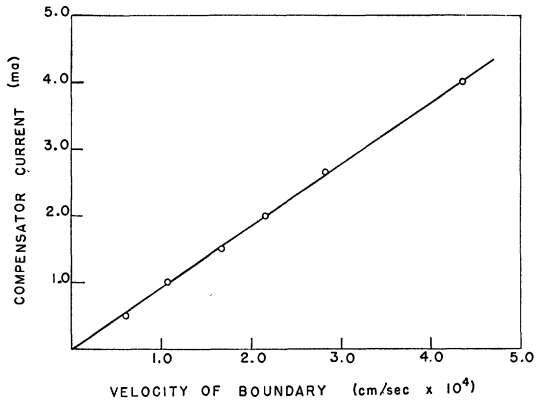

FIG. 2. Movement of a boundary formed between a 0.6% solution of ground nut globulin in phosphate—NaCl buffer (pH, 7.98; ionic strength, 0.10) and the same buffer under the influence of the compensator alone.

identical with that in the electrode vessels is injected into that vessel. However, in a simpler form of the apparatus, in which a glass tube leads directly from the base of A to the electrode vessel, the electrolyte solution

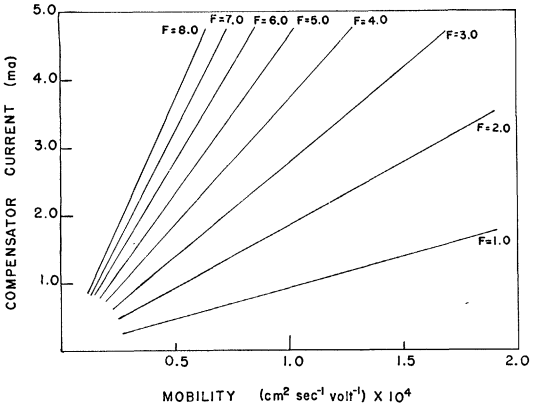

FIG. 3. Calculated mobility/compensator current for exact compensation of boundary used to obtain Fig. 2, at field strengths from 1.0 to 8.0 v/cm. F = field strength.

in A is expelled into the electrode vessel. The former arrangement is, in general, preferable. It is not essential that the injector be fitted before an experiment commences, since it is found that the disturbance to any boundary on gently dipping the nozzle just below the surface of the buffer in the electrode vessel is negligible.

The injector may best be calibrated by observing the motion of a protein boundary under its influence alone, when a graph of the type shown in Fig. 2 is obtained. It is then possible, using the usual relation,

$$\text{Mobility } (\text{cm}^2\ \text{sec}^{-1}\ \text{volt}^{-1}) = \frac{\text{velocity (cm/sec)}}{\text{field strength (v/cm)}},$$

to construct (cf. Fig. 3) a series of linear plots of actual mobility against compensator current for exact boundary compensation at the field strengths more commonly used in electrophoresis. Mobility determinations by this method are only very approximate, and it is more convenient to use the graph of Fig. 3 to estimate the compensator current required to hold a boundary nearly stationary. The duration of the injector depends solely on the volume of the bulb. For example, a short calculation will show that for an additional path length of 8.0 cm the total volume must be in excess of 12 cc. Since the volume may comfortably be 100 cc, the electrolytic compensator will suffice for the longest experiment.

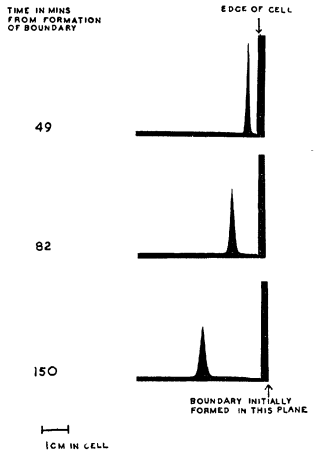

FIG. 4. Boundary formed between 0.6% bovine serum albumin in barbiturate buffer (pH, 8.15; ionic strength, 0.04) and the same buffer, displaced by the compensator. Compensator current, 3 ma.

An important property of the apparatus is the readily continuous control of the compensation afforded by the electrolysis. It has been used successfully to migrate protein components (of concentration down to 0.2%) over equivalent path lengths of 12 cm. At higher compensator currents it has also been used to move the protein boundaries backward to the center flange of the short section cell and hence to isolate the slowest and fastest components in the anode and cathode limbs. When the Tiselius cell is being used (without the electrode vessels) as a diffusion cell, a secondary attachment to the framework allows the nozzle of the compensator to be brought directly into one limb of the top section of the U tube. The boundaries formed in the flanges can then be moved smoothly through several centimeters to their observation positions (see Fig. 4)—a most important factor in diffusion work.

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