

particular coating granulation required to give optimal core centration.

7. Optimal core centration is desired for several reasons, the major ones being (a) Uniformity of dose, *i.e.*, if the tablets were to be broken along a center bisection, unequal doses would be obtained if the core is not in the center of the tablet. (b) Protective action of coating, *i.e.*, if the coating is used to improve the stability of the core ingredients, conceal the bitter taste of medicaments used in the core, and the like, the coating must completely cover the core tablet, otherwise the effectiveness of the coating is reduced. (c) Physical appearance, *i.e.*, if the core was to protrude out of the coating, either due to tilting or displacement in the vertical

plane or horizontal dislocation, it would give an unsatisfactory aesthetic appearance.

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Study of the Thermistor Bridge for the Measurement of Colligative Properties

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Further refinement of the apparatus described by Goyan and Reck has been studied, using thermistors. One variation described involves the use of intermittent power with simultaneous recording. Another variation treats the problem of using relatively high battery voltages in order to increase the sensitivity of the bridge without the use of amplifiers. The paper discusses the determination of molecular weights, as well as osmometry and isotonicity measurements. Results indicate that significant measurements can be made without minimizing the heating produced by the bridge current.

THERMISTORS may be used as resistance thermometers with high negative temperature coefficients. Because of their small size and low cost as compared to platinum resistance thermometers and their high coefficient; they seem to be ideally suited to the determination of temperature changes associated with freezing-point lowering and boiling-point elevation. One of the authors (1) has described an isotonicity meter based upon freezing-point measurements which includes a single thermistor in a Wheatstone bridge. The off-balance condition of the bridge is read on a vacuum-tube voltmeter. Ballard and Goyan (2) have shown that isotonicity in terms of per cent sodium chloride is a linear function of the usual colligative properties within the range of concentration and accuracy normally required.

It is quite proper to generalize that any osmometer, within the special limitations of each instrument, measures some approximately linear function of the colligative properties of solutions. The Hill-Baldes thermoelectric osmometer is no exception. In its original form it consisted of a thermocouple arranged in a constant temperature humidified air chamber (3). By placing a drop of solvent on one junction of the thermocouple and a drop of solution on the other, a temperature increase of the drop of solution relative to the drop of solvent develops measurable thermal E.M.F. This temperature difference and the resulting E.M.F. is proportional to the isotonicity or osmolal concentration of the solution.

With the advent of thermistors, many investigators (4-6) have modernized the Hill-Baldes osmometer by placing two thermistors in the chamber and connecting them as two arms of a Wheatstone bridge. This change has the advantage that the electric circuits are easier to

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deal with because of the higher voltage generated per degree of difference in temperature. However, the disadvantage of thermistors over thermocouples is that the former are heated by the current needed to operate them. This problem has been mentioned by most investigators. Their assumption that the heating effect may safely be neglected seems to be justified by their results. However, the present study has shown that good results can be obtained when the heating produced by the measuring current is greater than that produced by the phenomenon itself.

Goyan and Reck (7) made a radical modification of the Hill-Baldes osmometer by placing the two junctions of their thermocouple in separate tubes, each lined with platinum gauze for the purpose of holding solvent as close as possible to the junctions. This method gave good results and suggested the idea that the method is essentially a modification of the boiling-point method for determining colligative properties. Higuchi, *et al.* (8), followed this idea to its logical conclusion by evacuating the chamber after placing their solvent and solution in contact with thermistors. By means of mechanical stirring, they were able to simulate boiling-point work at room temperature and show that their results could be treated by classical thermodynamics.

When the need for accurate molecular weight determinations came to the attention of one of the authors, it was decided to modernize the Goyan-Reck apparatus by using thermistors. The present paper deals with this phase of molecular weight studies. It is obvious that any adequate measure of colligative properties will give a real or (in the case of dissociating or associating solutes) an apparent molal concentration. Since the weight of solute is known for some given quantity of solvent and the number of moles of solute in the same quantity of solvent is easily read from a suitable calibration chart of the instrument, it follows that the Goyan-Reck apparatus should be as effective in determining molecular weight as in determining isotonicity values.

This research began in an exploratory way. The first phase represents various attempts to minimize heating effects due to current through the thermistors. The second phase is a deliberate attempt to operate the thermistors at high current in order to take advantage of the greater sensitivity at the higher bridge voltages.

EXPERIMENTAL

Figure 1 shows the final modification of one of the sample cells using thermistors. During the first phase of this investigation, the tubes were 9.5 cm. long. Both were slipped through holes in a rubber

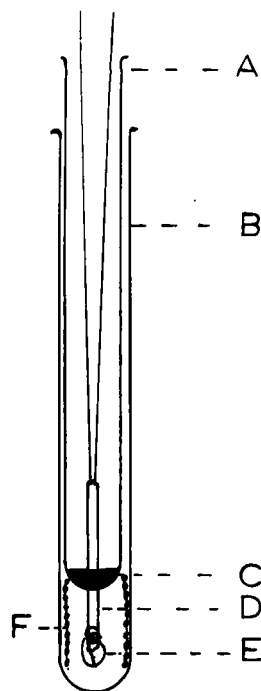


Fig. 1.—Thermistor assembly used in a constant temperature water bath maintained at 25° (about 5° above room temperature). A = glass tube supporting thermistor; B = glass tube selected so the thermistor support barely clears (7.5 mm. x 12 cm. I.D.); C = dental amalgam holding thermistor in place; D = thermistor as supplied at the end of a glass rod; E = platinum loop; F = platinum gauze.

stopper into water in a wide-mouth, 400-ml. Dewar filler having an internal diameter of 4.5 cm. The water in the Dewar flask was stirred vigorously with a stirring motor and a screw or propeller at the end of a free shaft. In the early part of the investigation it was thought desirable to adjust the temperature by changing the rate of stirring, but later a small coil of resistance wire (about 10 ohms) was wound inside a glass tube to serve as a heater. The heating was controlled manually by means of a variable transformer connected to a low-voltage transformer. When manual control of temperature became arduous, a thermocap relay was arranged to short an adjustable resistor in series with the heater. It was found that the value of this resistor should be such that the change in temperature was extremely gradual. Under these conditions, temperature corrections could be made for variations of 0.01–0.02°. Temperature was read on an 18–28° thermometer graduated in 0.01° marks. The same thermometer also served to operate the thermocap relay.

The electrical circuit for the first phase of the investigation has been described previously (9). The thermistor¹ used for the sample had a temperature coefficient of –4.8% per degree and a resistance

¹ The thermistors were type 51A1 from the Victory Engineering Corp. of Union, N. J., although not specially selected.

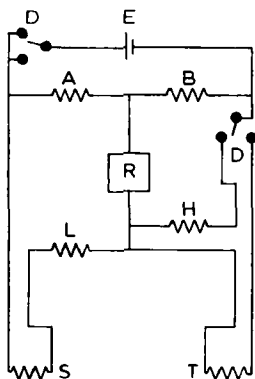


Fig. 2.—Circuit diagram of the bridge used for the high voltage work. A and B = ratio arm box; D = D.P.D.T. switch; E = battery (see text); H = Heathkit decade resistance box, 0-99,999 ohms; L = Leeds and Northrup box (see text); R = Leeds and Northrup Speedomax recording potentiometer 0-10 mv.; S = thermistor used for sample; T = thermistor used for reference.

of about 94,000 ohms at 25°. The ratio-arm box was used at the 1,000 settings. The switch built into the recorder for making and breaking external circuits was described in connection with incremental titration (9). This switch was used to open and close the battery circuit of the bridge at regular intervals, the closed condition lasting for a few seconds and the open condition about half a minute. Each time the battery circuit was closed the recorder would draw a horizontal line, the length of which was found to be a measure of the off-balance condition of the bridge. Consequently, the length of the lines for various known concentrations could be plotted against concentration in order to obtain a calibration chart.

Samples were added with a medicine dropper to the platinum loops surrounding the thermistor after removing the tube from the bath. A small piece of sheet brass was bent to form a channel to assist in removing the thermistors from the tubes without touching the sides. A slot was cut for the lip of the tube and the upper half above the slot built up with tape so that the surface of the tape was flush with the inner surface of the tube. The thermistor, after washing and filling, was replaced in the tube and the tube replaced in the water bath. During this operation the thermistors were connected but the battery circuit was open.

Figure 2 shows a circuit diagram of the bridge used in the second phase of the work. The positions of the battery and of the recorder were exchanged in developing this circuit from the one previously published (9). This was done in order to gain sufficient sensitivity without the amplifier. During a few experiments, a 10,000-ohm resistor was added to each ratio arm, but most of the work was done with the same 1,000-ohm ratio-arm resistors used previously.

It must not be assumed that the experimental details given above represent the authors' recommendation for a finished instrument. The object of the work was to study the design problem and to report significant information. For example, the switching arrangement designed to substitute a

resistance box for the thermistor used as a reference resistor was a great convenience in measuring absolute temperature changes, but did not contribute to the functioning of the instrument as an osmometer.

All solutions used were prepared by weighing chemicals from good quality commercial samples on an analytical balance. All of the solutions were made with distilled water as the solvent and distilled water was always used on the reference thermistor.

RESULTS

Phase I

The first phase of the work showed that thermistors could be substituted for thermocouples in the Goyan-Reck apparatus without reducing sensitivity. The advantage of this substitution is that there is no need to take great pains to avoid parasitic thermal potential differences, thus eliminating the critical need for a constant-temperature air bath. It was further established that when the current from a 1½-v. battery passed through the bridge for a few seconds at half-minute intervals, the line drawn by the recorder pen varied in length as a function of the off-balance condition of the bridge. Within limits, the length of these lines is a linear function of the concentration of solution on the sample thermistor. Figure 3 shows a typical recording and Fig. 4 shows the accumulated results of several measurements.

The feasibility of this intermittent method is interesting, but it failed to produce a dramatic improvement in results over what might be expected from a thermocouple and a good amplifier. It was discovered that the limit of accuracy was determined by the geometry of the drop with respect to the platinum gauze, the design of the water bath, rate of stirring, and freedom from rapid temperature changes in the bath. One important

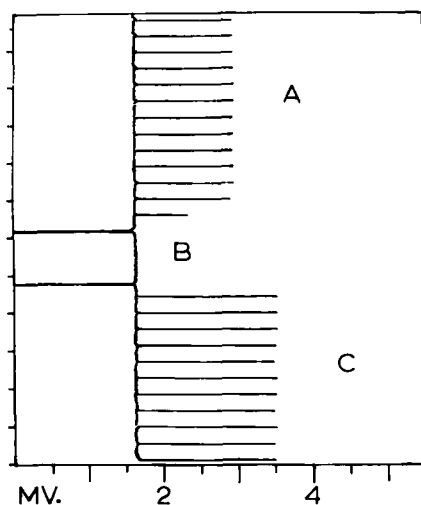


Fig. 3.—A typical recording using the intermittent method at 1½ v. on the bridge. The graph shows millivolt values at regular time intervals. A = water; B = open circuit; C = 0.0435 M dextrose. Each division on the ordinate represents approximately 100 sec.

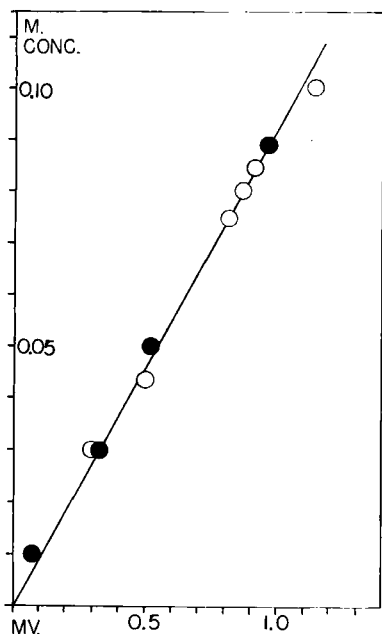


Fig. 4.—Calibration chart for the intermittent method: ●, sucrose; ○, dextrose. (Molar concentration vs. difference between mv. reading for water and solution.)

consideration in the design of the water bath is that there should be an air space between the rubber stopper and the surface of the water, thus indicating that the use of a Dewar flask is important.

Phase II

The second phase of this study was suggested by the results of the first. Substitution of thermistors in place of thermocouples made it possible to simplify the electrical circuit. It seemed reasonable to explore the use of higher battery voltages across the bridge so as to obtain greater off-balance voltage for the same change in thermistor resistance. It is easy to show that, to a good approximation, for a balanced bridge of the type shown in Fig. 2

$$\Delta E = \Delta R(E/4R)$$

ΔE is the potential difference seen by the recorder; E is the battery voltage; R is the resistance of either thermistor arm; and ΔR is a small change in R . This equation was verified in practice. One-hundred ohms variation of the box in series with the sample thermistor showed 1.4 mv. for a 6-v. battery, 2.9 mv. for a 12-v. battery, and 5.9 mv. for a 24-v. battery.

The easy conversion from millivolt reading to ohms is a great help in reading the bridge. It is not necessary to balance except to the nearest 100-ohm setting. Two positions on the recorder chart separated by the voltage corresponding to 100 ohms are located to the right and left of the nul position by approximately balancing the bridge. The exact resistance required to balance is then easily calculated.

The use of the recording potentiometer as a nul instrument for a Wheatstone bridge would seem needlessly complex except for the fact that the

equation given above is valid only when very little current is flowing through the nul instrument. Another and more essential use of the recorder is to establish final equilibrium values. Figure 5 shows a typical example of a slow and a moderately rapid rate of attainment of equilibrium after the sample had been exposed to the air of the room. Solutions seem to come to a steady state more slowly than pure water, indicating that in some cases diffusion of a film of condensed water is a problem when the drop was initially cooled by evaporation. The general behavior of the samples indicates the desirability of making a hole close to and parallel to the thermistor through the glass tubing support in order to insert a long hollow needle for washing and filling without removing the thermistor from the bath. This is an excellent feature of a commercial instrument (10). An innovation which seems to hasten equilibrium is to wait a few minutes before connecting the battery to the bridge. Convection caused by the heating of the thermistor probably provides some convection stirring which differs under different conditions.

The method used for placing the sample has some advantages, however. It is simple and makes it easy to wash and dry the thermistor before adding a sample, thus reducing the volume of solution required to about 0.1 ml. For exploratory work of the type reported, there is considerable advantage in frequent inspection. Several experiments with solutions of potassium permanganate showed that one of the platinum loops could be washed with 10–20 drops of new solution.

The most important conclusion that can be drawn from this work is shown in Fig. 6 and Table

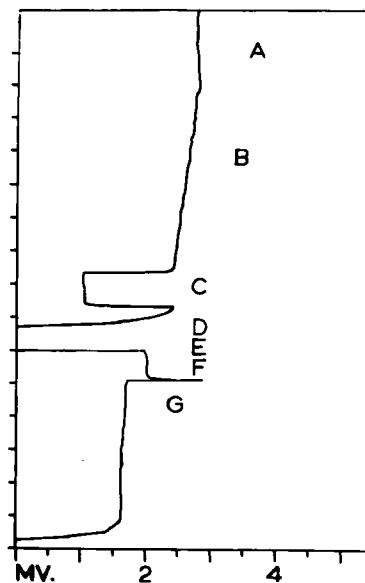


Fig. 5.—A typical recording using 6 v. across the bridge. (Time vs. mv.) A = final value for 0.1 M urea; B = slow attainment of steady state; C = change of decade box by 100-ohms; D = rapid approach to approximate equilibrium; E = thermistor first connected; F = battery circuit open; G = final equilibrium value for water. Each division on the ordinate represents approximately 100 sec.

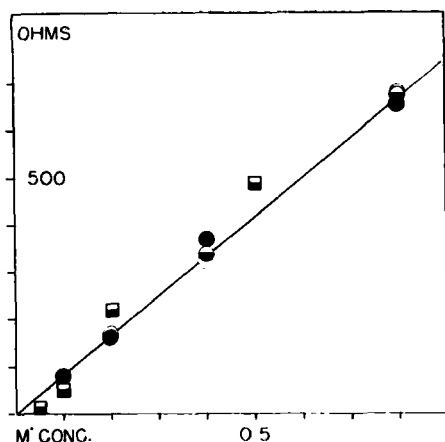


Fig. 6.—Cumulated results at several different battery voltages. Open figures = 6 v., half-open figures represent 12 v. and dark figures represent 24 v. Circles represent urea; and squares, sucrose. Molar concentration is plotted against the difference between water and solution in ohms

I. It will be noted that high voltages across the bridge can be used without evidence of serious trends. The temperatures shown in Table I were

TABLE I.—A STUDY OF AQUEOUS SOLUTIONS OF UREA AT DIFFERENT BATTERY VOLTAGES^a

M	Resistance Change from Value with Water, ohms		
	6 v.	12 v.	24 v.
0.1	72	69	82
0.2	159	167	160
0.4	319	337	371
0.8	685	676	650

^a Temperature elevation due to current: 0.07° at 6 v., 0.20° at 12 v., 0.63° at 24 v.

calculated from data taken with the bath at 25° and the resistance box substituted for the standard thermistor. Water was placed on the sample thermistor and readings taken at different bridge voltages. The first reading at 1½ v. was taken as the true resistance of the thermistor at 25°. As the voltage on the bridge was increased, the resistance went down. The differences were converted to temperature from the measured temperature coefficient and resistance of the thermistor.

Although there seems to be no evidence that the results obtained with high voltage across the bridge are invalid, there are some anomalous results that may indicate that the steady states developed on the thermistor are influenced by other factors.

This has been recognized for some time (3), and it is possible that the excessively warm drops amplify this effect. Figure 6 displays the results obtained with sucrose. It will be noted that the points for this substance deviate from a straight line by an amount greater than can be attributed to experimental error.

DISCUSSION

This work is of value in the development of improved instrumentation based upon the Hill-Baldes principle, although the authors are not presenting a finished instrument. It is of special interest that high voltages can be used successfully even though the resulting heating of the thermistor amounts to a change of resistance of almost 3,000 ohms or nearly three-quarters of a degree.

Neither method was pushed to its fullest extent either with respect to accuracy or convenience. However, a study of the data used to plot Fig. 4 shows an average deviation of 1.5% for the three points above 0.01 M. All of the dextrose points show an average deviation in the calculated slope of a hypothetical straight line of 3.6%. It is safe to conclude that routine measurements could be made with less than 3% error for the intermittent method.

No attempt was made to refine the techniques used in obtaining data for Table I. Most of the values reported were obtained from duplicate determinations. The maximum difference was 14%, the minimum difference was 0.3%, and the average difference was 5%. This was sufficient to show a lack of significant trend as a function of battery voltage and indicated that the use of higher current might be expected to give satisfactory molecular weights. A systematic determination of the molecular weight of an unknown compound using a 6-v. supply showed an average deviation of 1.8% for nine readings. It is not to be assumed that this value necessarily represents the ultimate accuracy obtainable.

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