Oesper Museum Booklets on
the History of Chemical Apparatus

No. 10

CLASSICAL MOLECULAR WEIGHT DETERMINATIONS

William B. Jensen
University of Cincinnati

Photography by Jay Yocis

Oesper Collections
University of Cincinnati
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SERIES INTRODUCTION

Like most museums, only about 25% of the holdings of the Oesper Collections in the History of Chemistry are on public display at a given time. In order to make the remaining 75% available in some form, it was decided to initiate a series of short museum booklets, each dedicated to a particular instrument or laboratory technique of historical importance to the science of chemistry. Each booklet would include not only photographs of both displayed and stored museum artifacts related to the subject at hand, but also a short discussion of the history of the instrument or technique and of its impact on the development of chemistry as a whole. Several of these booklets are expansions of short articles which have previously appeared in either the bimonthly series *Museum Notes*, which is posted on the Oesper website, or the series *Ask the Historian*, which appeared in the *Journal of Chemical Education* between 2003 and 2012.

William B. Jensen
Cincinnati, OH
April 2014

Introduction

Molecular weights were of no interest to chemists until the advent of John Dalton's (figure 1) atomic theory in the first decade of the 19th century, when they became relevant in two distinct ways. The first of these has to do with the fact that calculation of a compound's compositional formula using atomic weights and gravimetric composition gives information on only the relative number of each atom present, rather than the total number.[1] Curiously this distinction does not appear to have been appreciated by Dalton. It was, however, fully

Figure 1. John Dalton
(1766-1844)

understood by Berzelius, who suggested use of the terms *relative formula* and *absolute formula* to distinguish the two cases. Currently, the terms *empirical formula* and *stoichiometric formula* are also used for the former case and the term *molecular formula* for the latter case.

The absolute formula of a species is always a whole number multiple ($x = 1$, 2, 3 ...) of its relative formula. The relevance of molecular weights to this important distinction results from the fact that what it true of the relation between a species' relative and absolute formulas is equally true of their corresponding formula weights:

x(relative formula weight) = (absolute or molecular formula weight)   [1]

Thus determination of a species' molecular weight is key to determining the value of x and the species' corresponding absolute formula. This facet of molecular weight determination would become particularly important after the rise of organic chemistry in the second half of the 19th century.

The second, and initially more important, use of molecular weights by 19th-

century chemists was as a possible pathway to the determination of atomic weights – an application that dominated the first half of the 19th century. This particular use has a complex history and requires several additional assumptions.[2] These will be touched on in the final section of this booklet. For the present, however, we will instead focus on the various techniques and apparatus developed during the 19th-century for the experimental determination of molecular weights.

Gas Density

The first person to argue that relative molecular weights could be calculated from gas densities was the Italian physicist, Amedeo Avogadro (figure 2), in his famous memoir of 1811:[3]

... the ratios of the relative masses of the molecules are then the same as those of the densities of the different gases at equal temperature and pressure ...

This conclusion followed directly from Avogadro's well-known hypothesis that:[3]

Figure 2. Amedeo Avogadro (1776-1856)

... the number of integral molecules in any gas is always the same for equal volumes [at the same pressure and temperature] or always proportional to the volumes.

As indicated by the descriptor "hypothesis," this was a theoretical assumption on the part of Avogadro rather than an experimental fact. However, at present, the same conclusion may be readily deduced from the experimentally-based ideal gas law:

$$PV = nRT \qquad\qquad [2]$$

where P is the pressure, V is the volume, T is the absolute temperature, n is the number of moles of gas present, and R is the universal gas constant. By substituting both the weight definition of a mole:

$$n = m/MW \qquad\qquad [3]$$

(where m is the mass of the gas and MW is its molecular weight) and the definition of mass density (ϱ):

$$\varrho = m/V \qquad\qquad [4]$$

into equation 2 and solving for the molecular weight, we obtain the result:

$$MW = \varrho(RT/P) \qquad\qquad [5]$$

which agrees with Avogadro's original conclusion that molecular weights and gas densities are directly proportional to one another at constant T and P.

Though Avogadro would return to the subject of molecular weights and gas densities in several later essays,[4, 5] he himself apparently never experimentally measured gas densities but rather relied on the values reported in the literature. Most of these involved species that are gases at room temperature and pressure (RTP), and were determined by first weighing a sealed container of known volume that had been evacuated and then
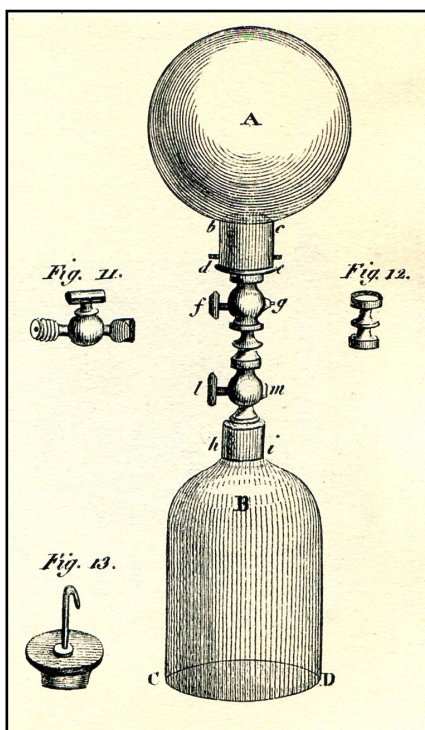

Figure 3. A glass ballon (A) attached to the gas receiver (B) for a pneumatic trough as depicted in Lavoisier's *Traité élémentaire de chimie* of 1789. Also shown are various alternative attachments for the balloon.

reweighing it again after filling it with the gas of interest at a given pressure and temperature. The container in question was usually a large glass or metal globe, called a balloon, that was equipped with a brass stopcock and a fitting that allowed it to be attached to either a vacuum pump, a gas receiver (figure 3), or to a brass hook in order to suspend it from one arm of a suitable balance when weighing it (figure 4). Using the difference between the mass of the evacuated versus the filled balloon presumably cancelled out the effects of air
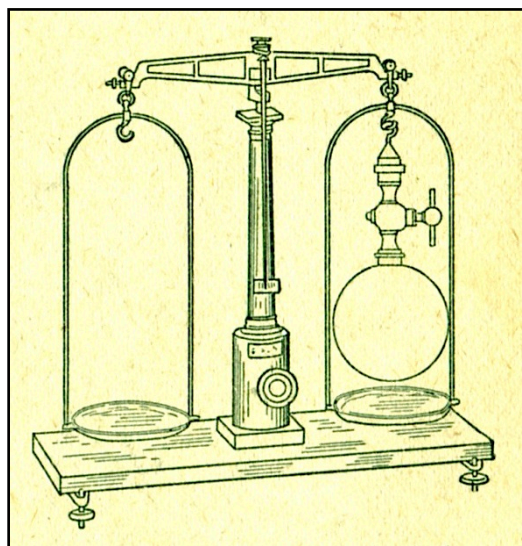

Figure 4. Weighing a glass balloon in order to determine gas density.

buoyancy and gave the mass of the gas present. This, when combined with the known volume of the balloon, allowed one to calculate the gas density at the temperature and pressure in question and thus the relative molecular weight of the gas.

Vapor Density

As already noted, the above procedure was normally applied to species that are gases at RTP. However, in 1826, and again in 1832, the French chemist, Jean-Baptiste Dumas (figure 5), extended this approach to the measurement of the high-temperature vapor densities of

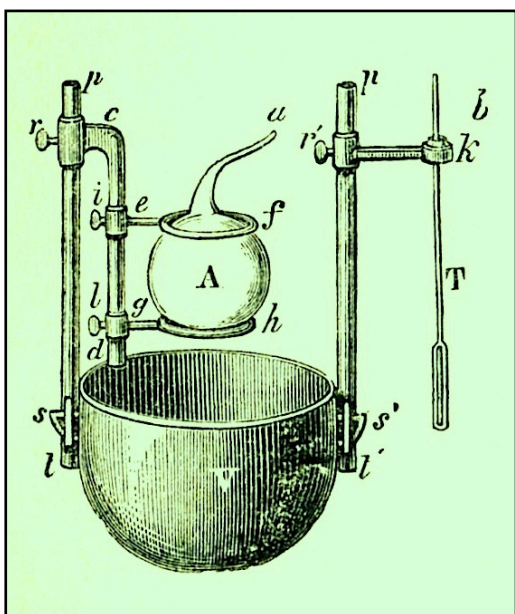Figure 5. Jean-Baptiste Dumas (1800-1884)

Figure 6. Dumas' circa 1832 modified apparatus for the determination of vapor densities. A is the glass bulb, V is the bath and T is the thermometer. The two vertical rods allow the bulb and thermometer to be raised from or lowered into the bath.

various compounds and simple substances that were normally either liquids or solids at RTP.[6, 7]

For this purpose he used a glass bulb with a neck that had been drawn out to a narrow opening and which was heated in either a water, sulfuric acid, or molten alloy bath (figure 6). As before, it was necessary to note the pressure in the laboratory, the temperature of the bath, and the mass of the empty bulb. The sample of interest was then added to the bulb and the latter heated in the bath until the sample was completely vaporized and had displaced any air present as indicated by disappearance of the schlieren lines produced as the vapor escaped from the narrow opening in the neck. This was the point at which the vapor in the bulb was in equilibrium with the external pressure in the room. The tip of the neck was then sealed shut with a flame and the bulb cooled to room temperature and weighed to determine the mass of the sample vaporized. The tip of the neck was then cut open, the bulb filled with water and both it and the removed tip carefully weighed in order to determine, using the known density of water, the volume of the bulb.

By the end of the 19th century the Dumas method was still being described in manuals dealing with so-called "physico-chemical measurements"[8, 9] and, at present, it is sometimes used as an experiment in general chemistry, where it is both scaled down and applied only to organic liquids with low boiling points. However, the method has numerous disadvantages, not the least of which was the necessity of using a fresh glass bulb for each determination and, starting in the 1880s, it was

largely displaced by a newer method for the determination of vapor densities introduced by the German chemist, Viktor Meyer (figure 7) in 1878.[10, 11] By this time the atomic weight problem has been resolved and molecular weights were now of most interest to the practicing organic chemist, since an absolute formula is a necessary prerequisite for the determina-
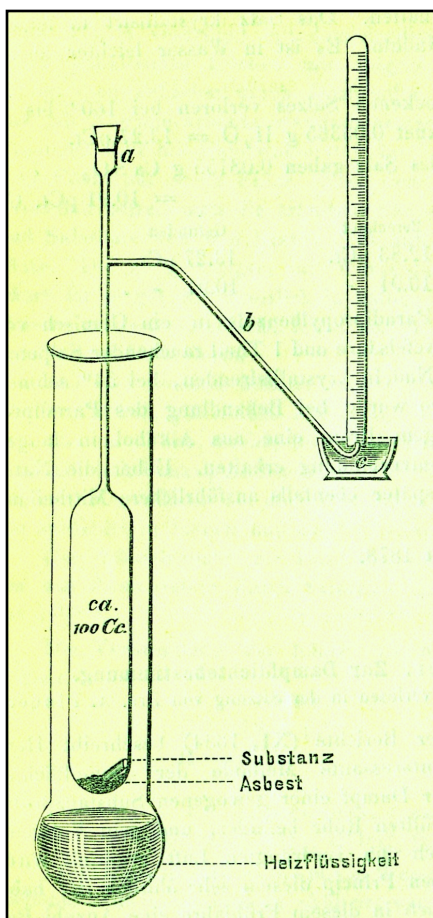

Figure 7. Viktor Meyer
(1848-1897)

Figure 8. Meyer's original diagram of his apparatus for the determination of vapor density.

tion of a species' classical structural formula.

Meyer's apparatus consisted of a long glass tube with a 100 mL bulb at the bottom, a stoppered opening at the top, and a side-arm that extended into a small pneumatic trough containing an inverted graduated glass tube as the receiver (figure 8). The tube and bulb were surrounded, in turn, by a larger tube contained a quantity of water or other suitable substance at the bottom which was converted to the corresponding vapor by heating with a Bunsen burner and which served to heat the bulb and its contents. The heated air in the empty apparatus was first allowed to come to equilibrium as indicated by absence of air bubbles exiting the side-arm into the pneumatic trough, after which the graduated

tube was introduced. The cork at the top of the apparatus was then briefly opened and a known mass of the sample, either in the form of a pastille, if solid, or contained in a tiny, loosely stoppered vial, if liquid, was dropped down the tube into the bulb, where its fall was cushioned either by a small pad of asbestos wool or a layer of sand. In the case of liquids, the increasing vapor pressure as the sample heated up would blow out the stopper of the vial and allow the bulb to fill with the sample's vapor. This would displace the heated air in the bulb and the displaced air would, in turn, displace the water in the graduated tube in the pneumatic trough. The volume of displaced air at RTP is equal to the volume of the sample vapor under the same conditions and simple substitution into the ideal gas law, in conjunction with the room pressure (corrected for the vapor pressure of water) and the sample's known mass, then allowed one to find the corresponding vapor density and molecular weight.

By the end of the century this method was not only routinely described in manuals dealing with physico-chemical measurements[12] but also in various laboratory manuals for organic chemistry[13] and for physical chemistry.[14] At present, however, it is no longer taught in undergraduate organic laboratory courses, where it has been displaced by discussions of more modern instrumental methods, such as IR, NMR, and mass spectroscopy, though, like the Dumas method, it is sometimes still used as an experiment in general chemistry.

Freezing-Point Depression

As a result of the studies of the French chemist, François-Marie Raoult (figure 9), the 1880s also saw the introduction of an entirely new set of methods for the determi-
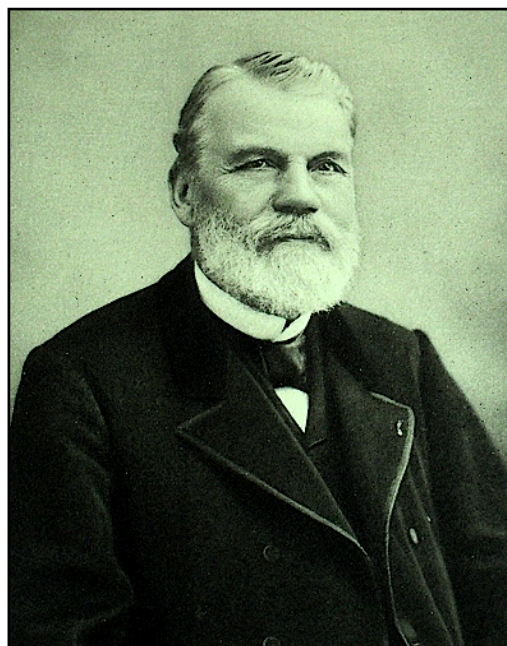
Figure 9. François-Marie Raoult (1830-1901)

nation of molecular weights, this time for various solutes species in liquid solutions rather than for gases and vapors. Both the fact that various solutes will lower the freezing point of a liquid solvent and the fact that the effect is proportional to the concentration of the solute have been known since the end of the 18th century.[15] Raoult, however, was able to quantify and generalize this effect in terms of the relative molecular compositions of the solutions rather than in terms of their composition by volume or weight, and verbally summarized his conclusion in 1882:[16]

One molecule of any compound dissolved in 100 molecules of any liquid of a different nature lowers the freezing point of this liquid by a nearly constant quantity close to 0.62 degrees.

At present this result has been recast in the form of the equation:
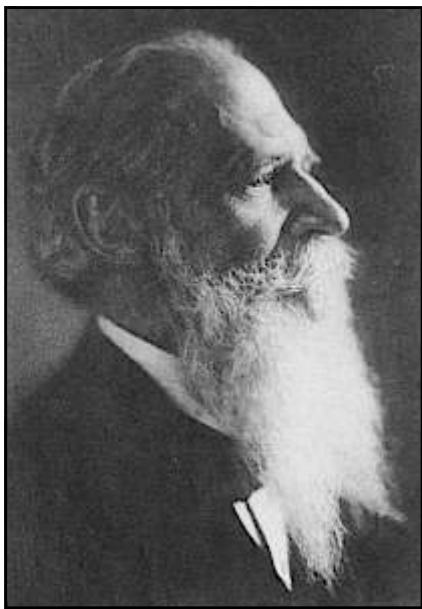
$$\Delta T_f = k_f b \tag{6}$$

Figure 10. Ernst Beckmann
(1853-1923)

where ΔT_f is the difference in the freezing point of the pure solvent versus that of the solution, k_f is a constant characteristic of the solvent in question, and b is the molal concentration of the solute. Substituting the definition of molality:

$$b = n_{solute}/1000m_{solution} = (m_{solute}/MW_{solute})/1000m_{solution} \tag{7}$$

into equation 6 and solving for the molecular weight of the solute gives:

$$MW_{solute} = (k_f/\Delta T_f)(m_{solute})/1000m_{solution}) \tag{8}$$

where the masses of the solute and solvent are both

in units of grams.

The development of a simple apparatus (figure 11) for the rapid measurement of ΔT_f for a solution for which k_f, m_{solute} and $m_{solvent}$ are all known was first developed by the German chemist, Ernst Beckmann (figure 10), in 1888 and has remained essentially unchanged even to this day.[17, 18] The determination of molecular weights via the measurement of freezing-point depressions is formally known as *cryoscopy*.

Vapor-Pressure Depression & Boiling-Point Elevation

Both the fact that various nonvolatile solutes will lower the vapor pressure of a liquid solvent and the fact that the effect is proportional to the concentration of the solute have been known since the work of Wüllner in 1858.[19] But once again it was Raoult who quantified and generalized this effect in terms of the relative molecular compositions of the solutions rather than in terms of their composition by volume or weight – a result which he verbally summarized in 1887:[20]

One molecule of a nonsaline substance dissolved in 100 molecules of any volatile liquid decreases the vapor pressure of that liquid by a nearly constant fraction close to 0.0105.

Figure 11. Beckmann's original apparatus for the determination of freezing-point depression.

And once again it was Beckmann who converted this result into a useable laboratory technique for measuring the molecular weights of solutes through his realization that boiling points are not only inversely related to vapor pressures but are far easier to measure in the laboratory.[21, 22] Thus, instead of measuring vapor-

pressure depression we now measure boiling-point elevation. In this form the law is expressed as an equation analogous to that given earlier for freezing-point depression:

$$\Delta T_b = k_b b \qquad [9]$$

where ΔT_b is the difference in the boiling point of the pure solvent versus that of the solution, k_b is a constant characteristic of the solvent in question, and b is the molal concentration of the solute. Substituting the definition of molality in equation 7 and solving for the molecular weight of the solute gives, as before:

$$MW_{solute} = (k_b/\Delta T_b)(m_{solute})/1000m_{solution}) \qquad [10]$$

Beckmann's original apparatus of 1890 for the determination of boiling points is shown in figure 12. Unlike his apparatus for the determination of freezing points, his boiling-point apparatus underwent many variations and improvements over the course of time, largely connected with attempts to minimize transient hot spots due to convection currents and superheating. A version first described by Fuchs in 1895 is shown in figure 13,[23] one designed by McCoy in 1900 in figure 14,[24] and one designed by Cottrell in 1919,[25] and modified by Washburn and Read the same year, in figure 15.[26]
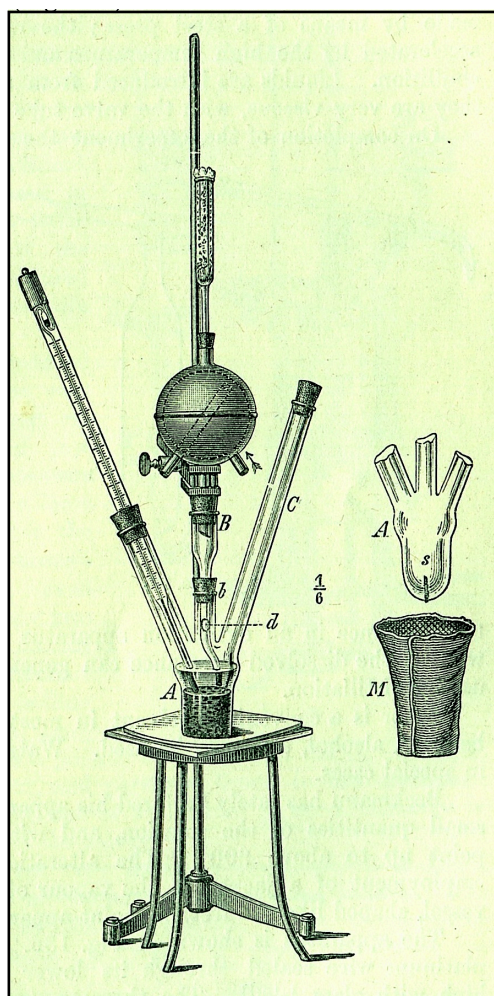
By the end of the 19th century, these

Figure 12. Beckmann's original apparatus of 1890 for the determination of boiling-point elevation.

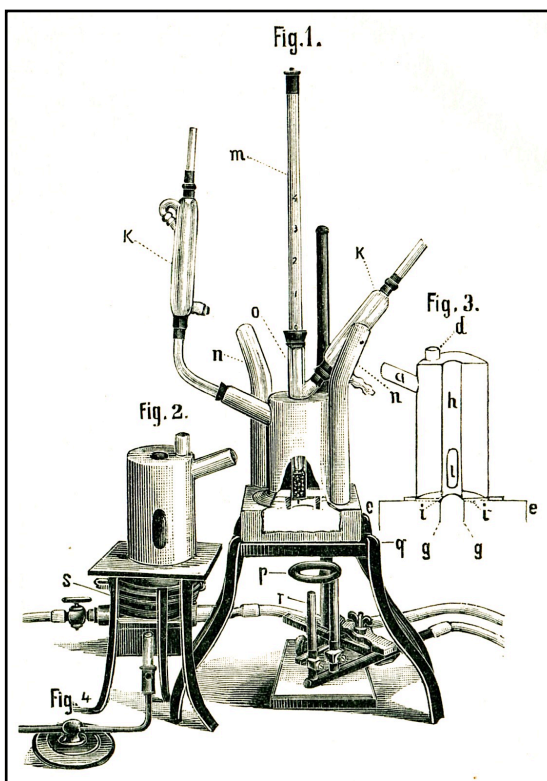solution techniques, like the earlier gas and vapor phase techniques, were not only included in various handbooks of physico-chemical methods and in various organic and physical chemistry laboratory manuals,[27] but were also the subject of speciality monographs.[23, 28-31] The determination of molecular weights via the measurement of boiling-point elevation is formally known as *ebullioscopy*.

Figure 13. Composite of some of the porcelain mantels for the determination of boiling point elevations as described by Fuch in 1895 and sold by F. O. R. Götze of Leipzig.

The Beckmann Thermometer

Both Beckmann's apparatus for the determination of freezing points and his apparatus for the determination of boiling points made use of an extremely sensitive adjustable difference thermometer of his invention (figure 16). The entire thermometer stem of about 50 cm length spanned only six degrees centigrade and was
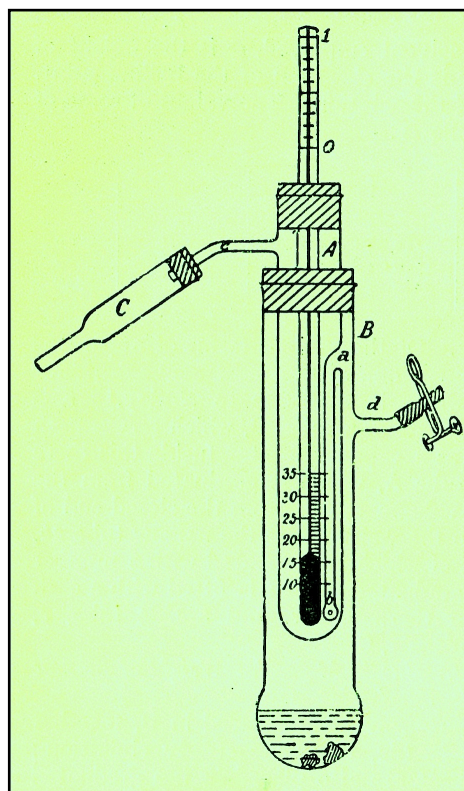

Figure 14. McCoy's apparatus of 1900 for the determination of boiling-point elevation.
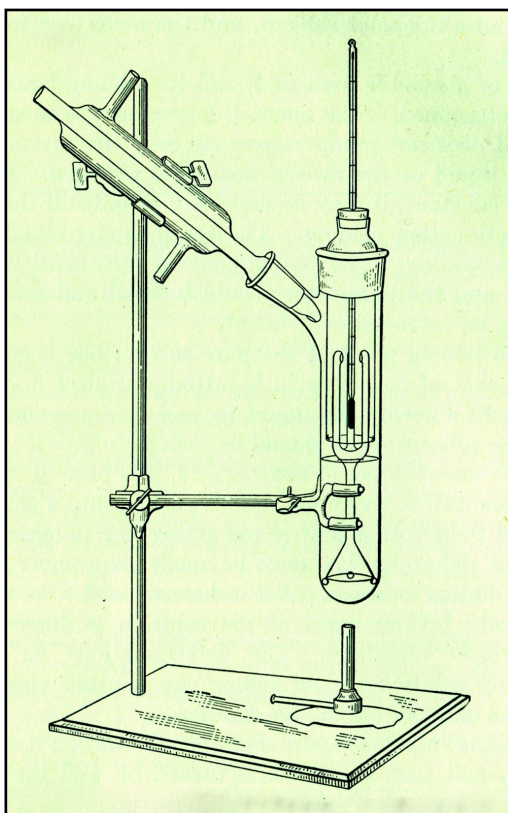
Figure 15. Cottrell's apparatus of 1919 for the determination of boiling-point elevation.

marked to the nearest hundredth of a degree, thus allowing one to estimate by eye to the nearest thousandth of a degree. Using the upper mercury reservoir, the thermometer was preset for the determination of freezing-point depressions at the six degree mark using a bath with a temperature corresponding to the solvent's known freezing point, whereas for the determination of boiling-point elevations it was preset to the one degree mark using a bath temperature corresponding to the pure solvent's boiling point.

Osmotic Pressure

If a concentrated liquid solution is placed in an inverted thistle tube (figure 17) whose mouth is covered by a semi-permeable membrane that allows passage of the solvent molecules but not the solute molecules, and this, in turn, is submerged in a container of pure solvent, the solvent will flow through the membrane from the pure solvent side to the solution side in an attempt to dilute the solution. The increasing volume of liquid on the solution side will force the liquid up the stem of the thistle tube, often to a height of several feet. The amount pressure that must applied at the top of the stem to prevent
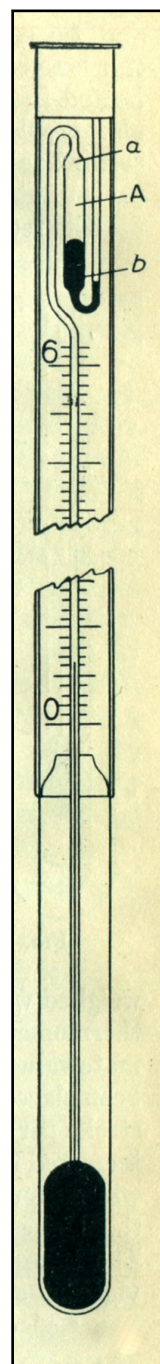

Figure 16. *Right:* A drawing of a typical Beckmann difference thermometer.

this solvent flow is known as the *osmotic pressure* of the solution.

Though long known, osmosis was first quantitatively studied by the German botanist, Wilhelm Pfeffer (figure 18), in a monograph published in 1877.[32] His apparatus was more complicated than the simple thistle tube device in figure 17 and consisted of a porous ceramic cup whose inner walls had been coated with a semi-permeable membrane of precipitated di-copper hexacyanoferrate(II). This container, after first filling with the solution of interest, was attached to a mercury manometer and sub-merged in a reservoir of pure water (figure 19).
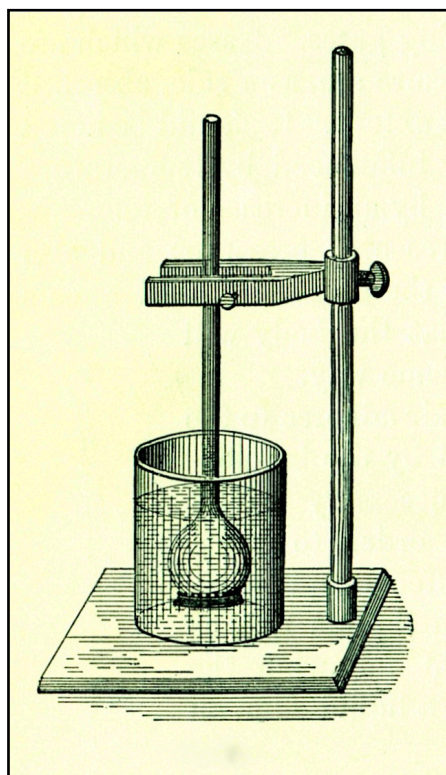

Figure 17. A simple device for demonstrating osmosis.

Thus, rather than measuring the pressure required to stop the osmotic flow, Pfeffer instead measured the height of the mercury column it could support.

Pfeffer expressed the concentrations of his solutions in weight percent and though he was able to confirm that the more concentrated the solution the greater its osmotic pressure, he was unable to deduce a simple quantitative law governing his observations. Rather it was the Dutch physical chemist, Jacobus van't Hoff (figure 20), who in 1887 showed that Pfeffer's data could be reformulated in the form of an equation analogous to the ideal-gas law (recall equation 2):[33]
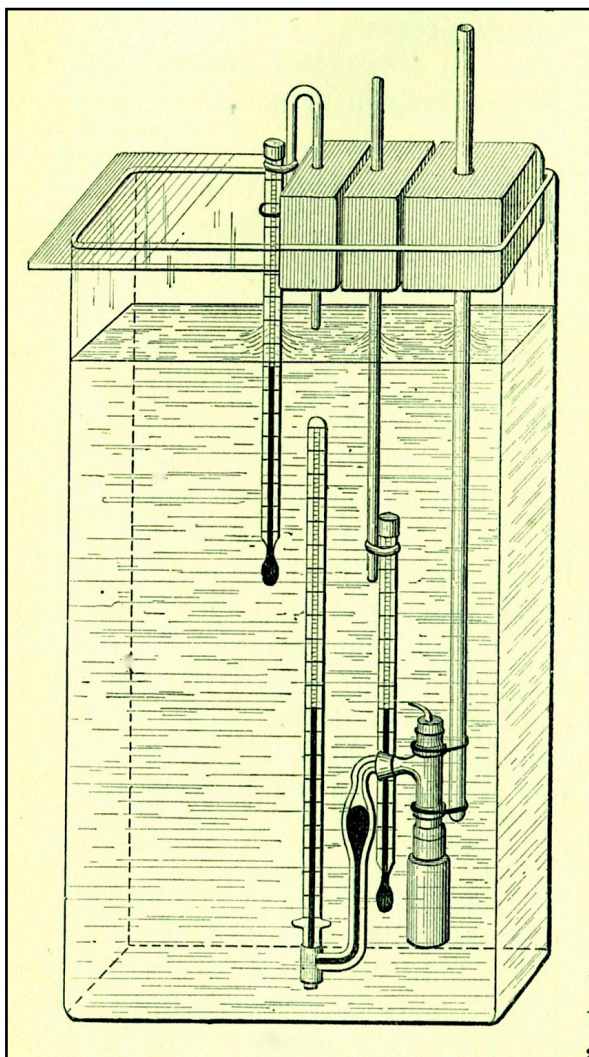

Figure 18. Wilhelm Pfeffer (1845-1920)

Figure 19. Pfeffer's 1877 apparatus for the study of osmotic pressure.

$$\Pi V_{solution} = n_{solute}RT \qquad [11]$$

where the osmotic pressure (Π) takes the place of gas pressure, solution volume ($V_{solution}$) the place of gas volume, and moles of solute (n_{solute}) the place of moles of gas. Substituting the weight definition of the mole in equation 3 and rearranging then gives the osmotic pressure analog of equation 5:

$$MW_{solute} = (m_{solute}/V_{solution})(RT/\Pi) \qquad [12]$$

Like the apparatus for the deter-
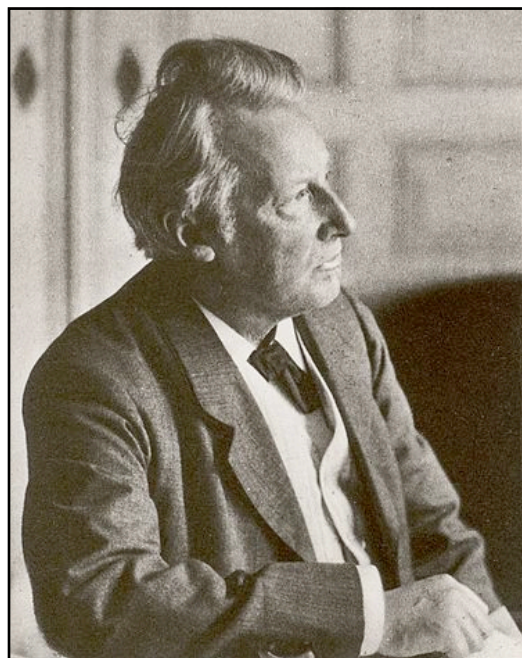
Figure 20. Jacobus van't Hoff (1852-1911)

mination of boiling-point elevations, apparatus for measuring osmotic pressures came in many forms. Figure 21 shows a typical example described by Findlay in 1913[34] in which the osmotic pressure was measured by the value of the external
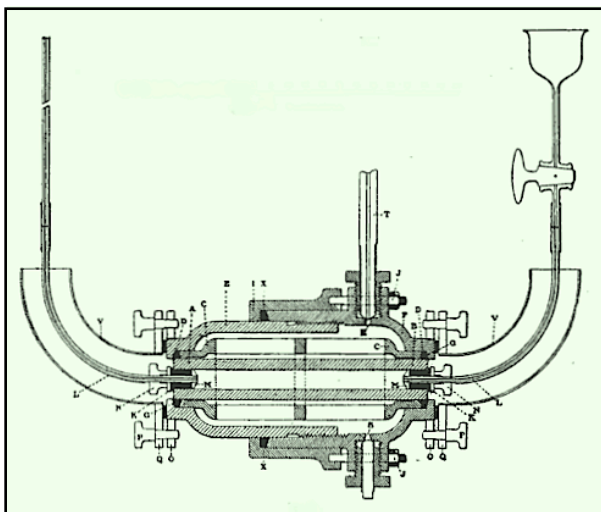
Figure 21. A high-pressure Berkeley-Hartley osmotic cell as described by Findlay in 1913.

pressure applied to the solution side of the membrane in order to prevent any solvent flow across the membrane. As may be seen from the cell's complexity, the required pressures were great enough to necessitate special seals and mechanical reinforcement of the membrane.

Unlike the other classical methods described earlier, the technique of osmometry was seldom discussed in detail in late 19th and early 20th-century handbooks on physico-chemical measurements or in typical organic and physical chemistry laboratory manuals – no doubt because of the experimental difficulties mentioned above. This is ironic, since, as we will see in the final section, even as most other classical methods gradually decreased in importance throughout the 20th century, osmometry would increase in importance, especially with regard to the fields of polymer chemistry and biochemistry.

Gas Effusion

A final classical method for determining the relative molecular weights of gases with low water solubility remains to be discussed, though it was never widely practiced. It is based on Thomas Graham's law of gaseous effusion. As first stated by Graham (figure 22) in 1833,[35] this referred to the relative volumes of any two gases, 1 and 2, that could effuse or escape through a small pinhole during equal time periods and stated that this volume for a given gas was "inversely proportional to the square root of the density of that gas." This may be expressed mathematically as:

$$(V_1/V_2) = (\varrho_2/\varrho_1)^{0.5} \qquad\qquad [13]$$

At present Graham's law is usually written in the form:

$$(rate_1/rate_2) = (\varrho_2/\varrho_1)^{0.5} = (V_1/t_1)/(V_2/t_2) \quad [14]$$

where the rate of effusion is defined as the volume of gas that effuses per unit time (t):

$$rate = V/t \qquad\qquad [15]$$

This reduces to Graham's original state-ment when comparing the differing volumes of various gases that effuse over equal time periods (i. e. when $t_1 = t_2$). However, if we instead compare the differing times required for equal volumes of various gases to effuse (i.e. when $V_1 = V_2$), then equation 14 becomes, on rearrangement:

Figure 22. Thomas Graham
(1805-1869)

$$(t_1/t_2) = (\varrho_1/\varrho_2)^{0.5} \qquad\qquad [16]$$

We know from equation 5 and the ideal-gas law that the ratio of the densities of any two gases at constant temperature and pressure is equal to the ratio of their molecular weights:

$$(\varrho_1/\varrho_2) = (MW_1/MW_2) \qquad\qquad [17]$$

Substituting this relation into equation 16 and solving for the ratio of the two mo-lecular weights, then gives us our final equation directly relating the ratio of the molecular weights to the square of the corresponding ratio of the effusion times for equal volumes of the two gases:
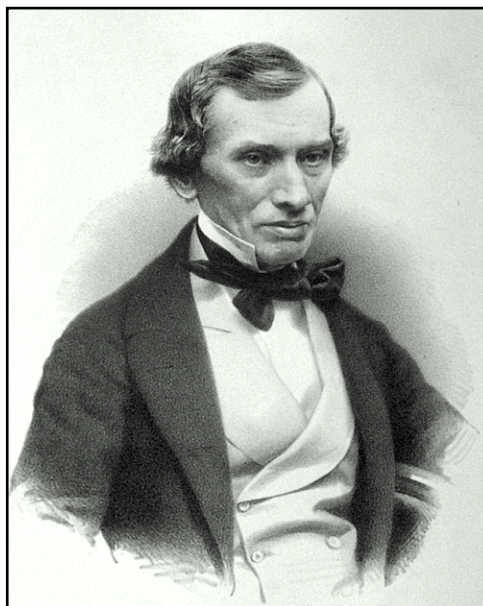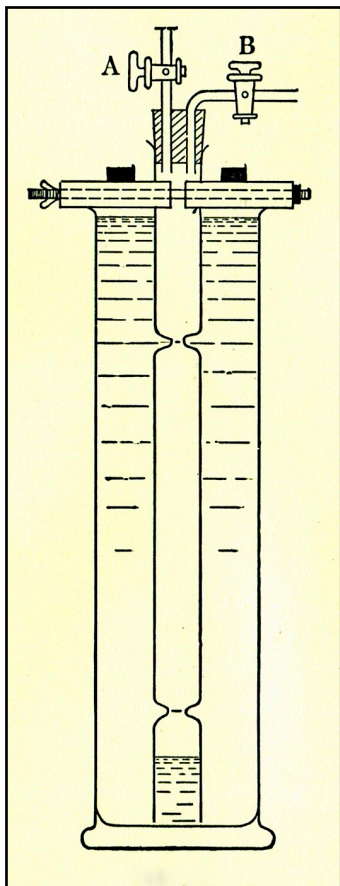
Figure 23. Schilling's apparatus for the determination of the molecular weights of gases via rate of effusion.

$$(MW_1/MW_2) = (t_1/t_2)^2 \qquad [18]$$

Equation 18 was made the basis of a simple apparatus (figure 23) for determining the relative times of effusion for equal volumes of different gases developed in 1879 by a German analytical chemist named N. H. Schilling and named in his honor.[36] This consisted of a glass cylinder with a second narrower cylinder inside marked with reference lines and/or contractions near both its bottom and top. The outer cylinder was closed at the bottom but open at the top, whereas the inner cylinder was open at the bottom and closed at the top save for two tubes, *A* and *B*, each with a stopcock. Tube *A* terminated in a piece of platinum foil containing a small pinhole, whereas tube *B* could be opened to either the air or connected to an external gas sample.

With both stopcocks open to the air, water was added to the apparatus until the inner tube was completely filled, at which point stopcock A was closed, tube *B* was connected to the gas sample, and the water in the inner tube displaced with the gas until it was even with the lower line. At this point stopcock *B* was closed and stopcock *A* opened so the gas could effuse through the pinhole. Recording the time required, the gas was allowed to effuse until the level of water in the inner tube reached the upper line. Comparing this time with that required for a sample of dihydrogen gas to do the same, then allowed one to calculate the molecular weight of the gas sample via equation 18.

In actual fact Schilling wasn't particularly interested in determining molecular weights but rather in rapidly characterizing the different gaseous components of coal gas, and it was only as part of a standard exercise for the physical chemis-

try laboratory that his apparatus was ever used for the former purpose.[37]

Museum Holdings

The museum owns either original or reconstructed examples of the apparatus required for all of the classical 19th-century methods of molecular weight determination described above, as well as several more recent examples of automated osmometers.

Figure 24. A 19th-century, 8 L, glass balloon with brass stopcock and weighing hook for the determination of gas densities. Compare with figures 3 and 4.

Figure 25. Gas receivers. The (6" x 16.5") example on the left is attached to a small metal balloon, whereas the (12" x 21") example on the right is sitting in an earthenware transfer basin. Compare the figure 3.

Figure 26. Circa 1960, 150 mL glass bulbs with glass stopcocks for the determination of gas densities, largely as an exercise for the undergraduate physical chemistry laboratory.

Figure 27. A reconstruction of a mid-19th century (7" x 10" x 24.5") Dumas apparatus for the high-temperature determination of vapor densities. The heat source is a Barthel alcohol blast-lamp. Compare with figure 6.

Figure 28. *Left:* A circa 1900 (11.5" x 18"x 37") Viktor Meyer apparatus for the determination of vapor densities. *Above:* Close-up of (0.19" x 1.25" and 0.13" x 0.88") vials for introducing liquid samples into the Viktor Meyer apparatus. Compare with figure 8.

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Figure 29. A circa 1960 (7" x 8" x 24") freezing-point depression apparatus with a spill pan. Compare with figure 11.

Figure 30. A (11" x 12" x 29.5") reconstruction of Beckmann's original apparatus of 1890 for the determination of boiling-point elevations Compare with figure 12.
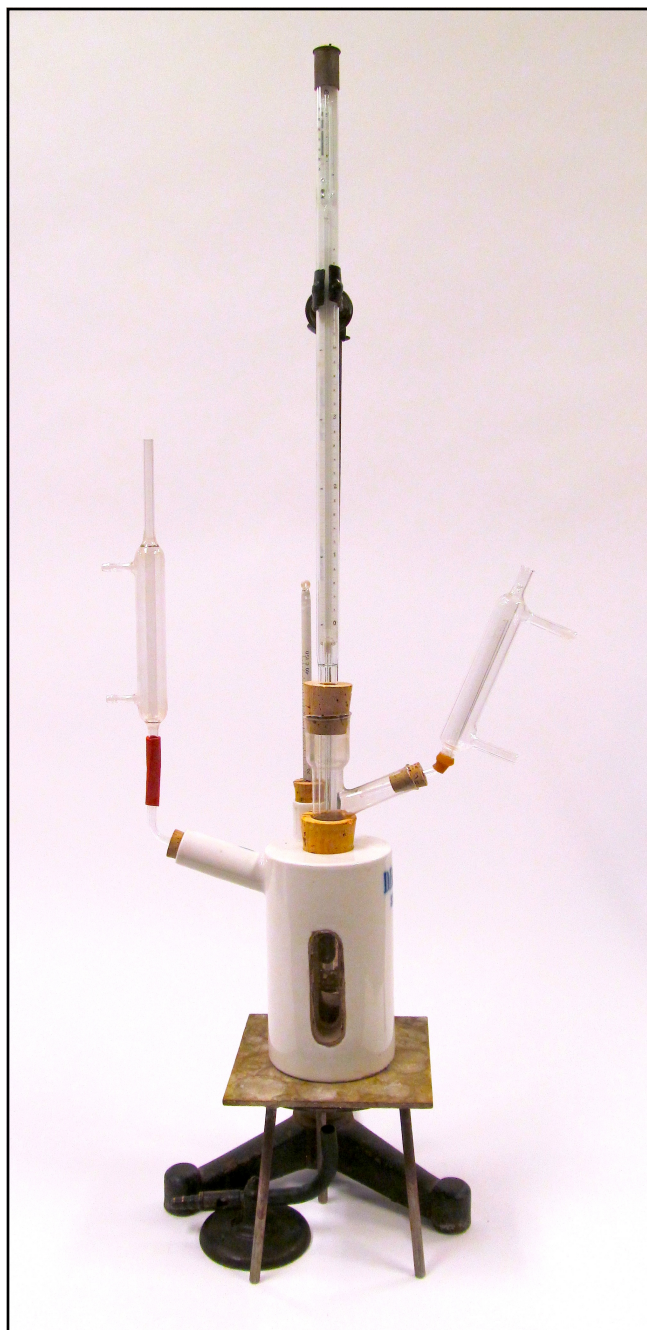
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Figure 31. A (11" x 12" x 30") boiling-point elevation apparatus as first described by Fuchs in 1895. The bath mantel is made of glazed porcelain with mica observation windows. Compare with figure 13. This was incorrectly identified on the original museum webpage.

Figure 32. A circa 1940 (7.5" x 12.5" x 29.5") version of McCoy's 1900 apparatus for the determination of boiling-point elevations. Compare with figure 14.

Figure 33. A circa 1940 (10.5" x 15" x 28.5") version of Cottrell's 1919 apparatus for the determination of boiling-point elevations. Compare with figure 15.

Jensen -Thomas Apparatus Collection

Figure 34. A circa 1940 (14" x 14.5" x 30.5") double-jacketed apparatus, presumably for the determination of boiling-point elevations, with an electrically heated vapor bath. Design origin unknown.
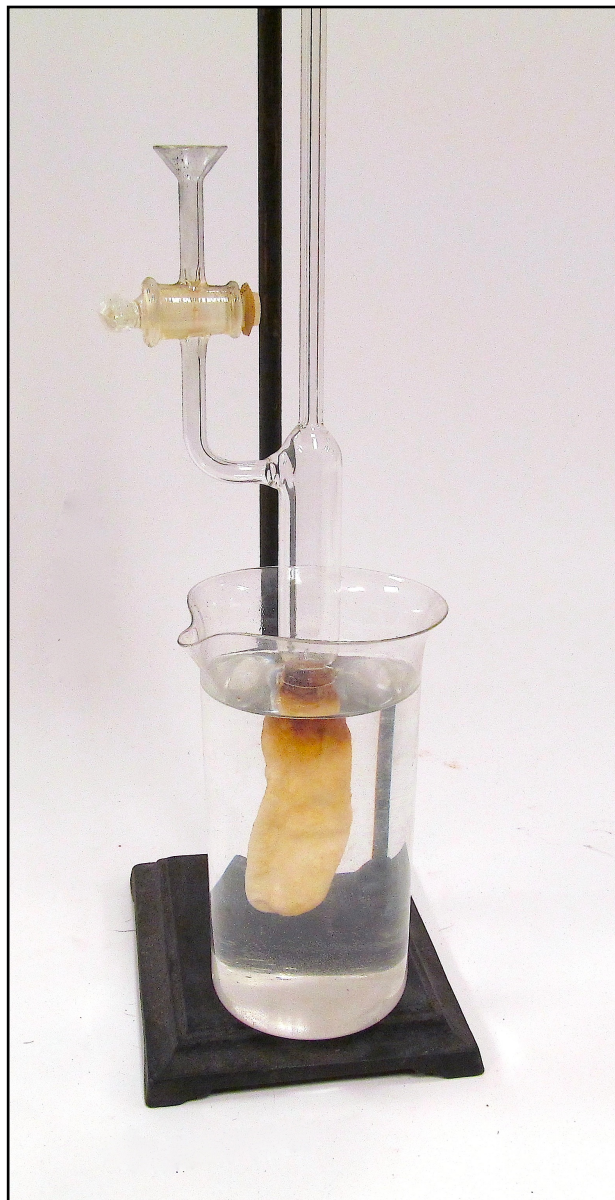
Figure 35. Closeup of the cell for a (0.75" x 3" x 54") class-room device for demonstrating osmotic pressure. The membrane bag has been tied to the open end of the solution compartment. This compartment can be filled via the funnel and stopcock on the left. The stem has been truncated in the photo since its overall height is around four feet. Generally Karo syrup, with a little dye added for better visibility, is used as the solution. This device is essentially a more sophisticated version of thistle-tube demo in figure 17.

Figure 36. Unglazed (3" x 6") porous ceramic flasks for use as high pressure osmosis cells after the manner of Pfeffer. These are listed twice in the circa 1920 catalog for the laboratory supply house of John J. Griffin and Sons of London – once under the heading of osmosis flasks and once under the heading of filter flasks.
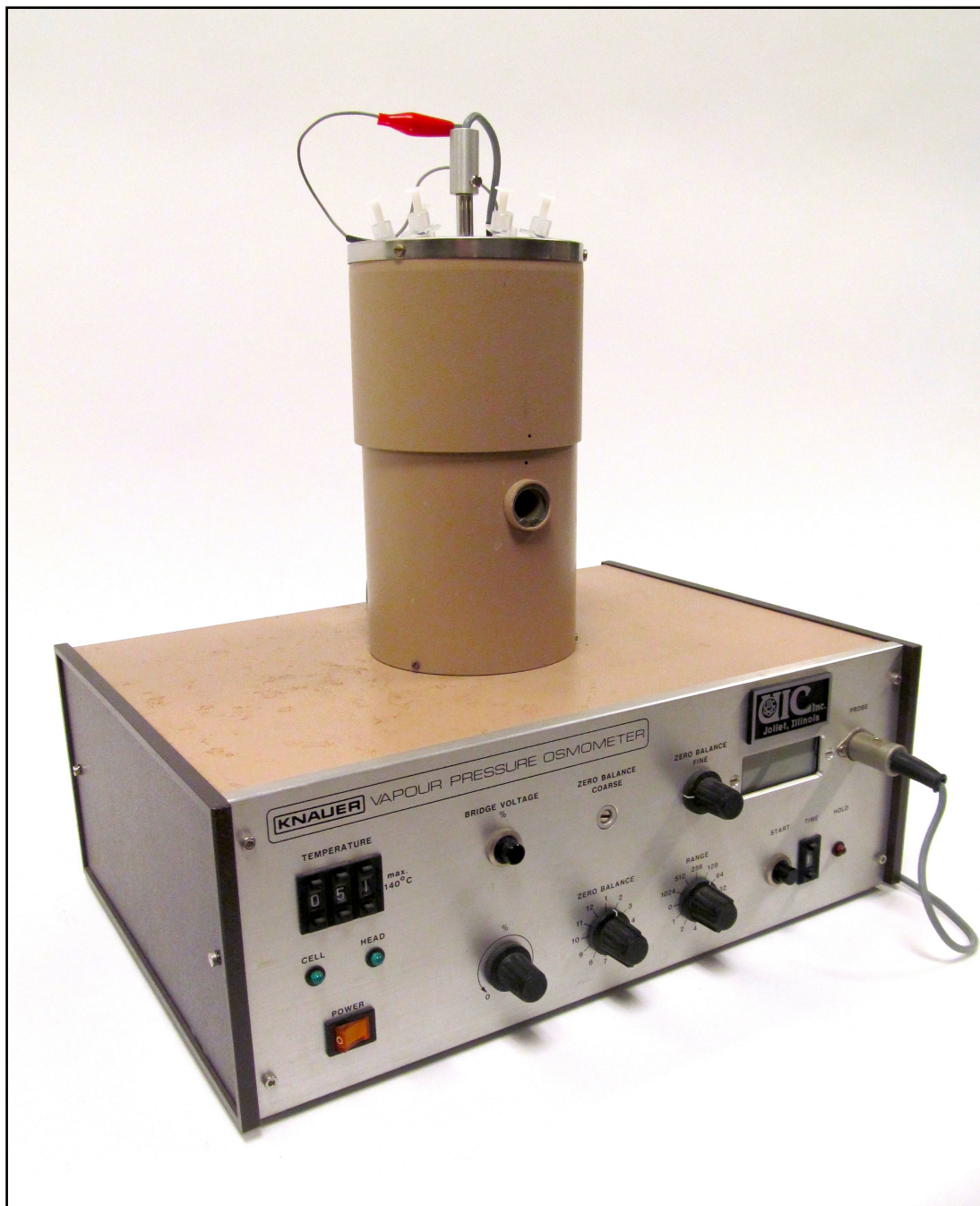
Figure 37. A circa 1980 (10" x 14" x 15.5") vapor pressure osmometer made by the German firm of Herbert Knauer of Berlin for the determination of molecular weights between 100 and 35000.

Figure 38. A circa 1970 (12" x 18" x 35") automated membrane osmometer made by Mechrolab Inc. of Mountain View, California. Shown sans power control and printer. Designed to measure average molecular weights between 20,000 and 1,000,000. See also figure 40.

Jensen -Thomas Apparatus Collection

Figure 39. A circa 1900 (6" x 7.25" x 24.5") Schilling apparatus for the determination of the effusion times and molecular weights of various gases. Note the reference lines at the bottom and top of the inner cylinder. Compare with figure 23.

The Significance of Molecular Weight Determinations in the History of Chemistry

As briefly stated in the introduction, the primary interest in molecular weight determinations during the first half of the 19th century was as a possible route to atomic weights, even though the extraction of atomic weights from molecular weights required additional theoretical assumptions and/or additional experimental data beyond those used to determine the molecular weights themselves. In the case of Avogadro, this additional experimental data was based on the reaction volumes of various gases measured by Gay-Lussac in 1808 in the course of formulating his well-known law of combining volume.[38]

Application of Avogadro's EVEN (**E**qual **V**olumes **E**qual **N**umbers) hypothesis to this data implied that the ratios of the experimentally measured reaction volumes of the various gases were a direct reflection of the ratios in which their component molecules reacted. Thus Gay-Lussac's result that one volume of hydrogen gas reacted with one volume of chlorine gas to produce two volumes of hydrogen chloride gas also meant that, at the molecular level, one molecule of hydrogen reacted with one molecule of chlorine to produce two molecules of hydrogen chloride. This can be expressed using a modern chemical equation as:

$$H_a + Cl_b \rightarrow 2H_{a/2}Cl_{b/2}$$
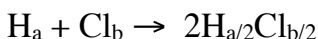
where Gay-Lussac's data and Avogadro's hypothesis have provided the molecular coefficients required to balance the equation, but the atomic coefficients are as yet to be determined.

To complete this determination Avogadro simply assumed that the missing atomic coefficients corresponded to smallest set of whole numbers required to complete the balancing of the equation, which, in this case, happen to be $a = b = 2$.[3] Thus it was that he postulated that the molecules in both hydrogen gas and oxygen gas were diatomic (H_2 and O_2) and that the true atomic weights of these elements were half of the numerical value of their molecular weights as deter-

mined from the measurement of their gas densities. Using a similar procedure for the reaction volumes found when hydrogen gas and oxygen gas react to produce gaseous water and for when hydrogen gas and nitrogen gas react to produce ammonia gas, Avogadro likewise correctly deduced that both oxygen gas and nitrogen gas contained diatomic molecules (O_2 and N_2). Unfortunately only a few elements form gas-phase simple substances at RTP and even fewer underwent gas-phase reactions for which the combining volumes had been determined, thus severely limiting the application of Avogadro's approach. This, however, did not deter him, and in later papers he used other theoretical assumptions in his ongoing attempt to extract atomic weights from molecular weights based on gas densities. Most of these were ill-founded and in the end he managed to propose more incorrect than correct atomic weights.[4, 5]

The same fate befell the French physicist, André-Marie Ampère, who in 1814 independently proposed both the EVEN hypothesis and the proposition that the molecules of simple substances could be polyatomic.[39] He felt he could extract atomic weights from molecular weights based on gas densities using a complex speculative theory of molecular geometry to determine the atomic coefficients for the molecules of simple substances – once more with the result that most of his values are now known to be incorrect.

Dumas was likewise unable to resolve the problem of determining correct atomic weights using the data obtained from his vapor density measurements.[6, 7] The molecular weight values found for mercury, phosphorus and sulfur were all at variance with Avogadro's diatomic result for the so-called permanent gases, since, as we now know, mercury is monoatomic in the gas phase (Hg), phosphorus is tetra-atomic (P_4), and sulfur may vary from octa-atomic (S_8) to hexa-atomic (S_6) to diatomic (S_2), depending on the temperature of the vapor. Most historians have argued that these apparently confusing results led to an eventual rejection of the EVEN hypothesis by Dumas and to his later skepticism concerning the atomic theory in general, though Rocke disagrees.[2]

Yet other chemists, such as Dalton and Berzelius, rejected the EVEN hypothesis because it conflicted, either explicitly or implicitly, with yet other theo-

retical assumptions and, rather than abandon these assumptions, they chose instead to reject Avogadro's hypothesis – a situation known among philosophers of science as the "Duhemian Pitfall."[40]

Resolution of this confusion is generally credited to the Italian chemist, Stanislao Cannizzaro (figure 40), who in 1858 published a lengthy paper entitled *Sketch of a Course in Chemical Philosophy*,[41, 42] reprints of which he distributed at a meeting of chemists who had gathered at Karlsruhe in 1860 to discuss how to resolve this very problem. In this paper Cannizzaro showed how to unambiguously determine atomic weights from molecular weights by combining the molecular weights determined from gas densities and the EVEN hypothesis with composition by weight data obtained via conventional gravimetric analysis.

Figure 40. Stanislao Cannizzaro (1826-1910)

Thus, for example, if one wished to obtain the atomic weight of chlorine, one first obtained the relative molecular weights for a series of gaseous chlorine compounds using gas densities, including that of the simple substance if possible (though this was not required if unavailable because of low volatility). As shown in the following table, each molecular weight was then multiplied by the weight fraction of chlorine present in the compound, as determined from its gravimetric analysis, in order to obtain what fraction of the molecular weight was due to chlorine alone. Whichever of these products had the lowest value was assumed to correspond to just one atom of chlorine until evidence to the contrary was found, and using this value to normalize the others then gave the chlorine atom count in each molecule. If, in measuring the relative molecular weights, one selected $MW_{Hgas} = 1$

Substance	MW on H gas = 2 Scale	Weight Fraction of Cl	Total Weight of Cl	Number of Cl atoms
Chlorine Gas	70.34	1.000	70.34	2
Hydrogen Chloride	36.17	0.972	35.16	1
Dichloromethane	84.75	0.830	70.34	2
Chloroform	118.42	0.891	105.51	3
Carbon Tetrachloride	152.59	0.922	140.67	4

as the standard, then the atomic weight of a chlorine atom came out as 17.59, whereas if one selected $MW_{Hgas} = 2$, then the atomic weight of Cl became 35.17 (recall that today these have been proportionately readjusted to 2.016 and 35.45 respectively). The $MW_{Hgas} = 2$ standard was the one selected by Cannizzaro, though it is important to note that, irrespective of which standard is used, the molecules in chlorine gas are always found to be diatomic.

Once the atomic weight problem was resolved, molecular weight determinations, as already pointed out, became of most importance to the organic chemist, who required them to convert the relative formulas obtained from gravimetric analysis into the corresponding absolute or molecular formulas via relation 1:

x(relative formula weight) = (absolute or molecular formula weight)   [1]

since these were a necessary prerequisite for further determining the structure of the molecule in question. Since accurate formula weights could now be calculated from the corresponding atomic weights obtained via gravimetric data, it was not necessary for the measured molecular weights to also be of high accuracy so long as they allowed one to unambiguously assign an integral value to *x* in this relation.

However, in the 1860s cases began to emerge of compounds for which the molecular weights obtained via gas densities failed to give an integral value for *x* and which, indeed, gave *x* values that varied with the temperature of the gas. It was soon established that the gases in question were undergoing a temperature-dependent partial dissociation. Thus, in the case of phosphorus pentachloride, the

gas was actually a mixture of the three chemical species in the equation:

heat + $PCl_5(g) \leftrightarrow PCl_3(g) + Cl_2(g)$
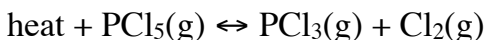
Detailed study of this reaction and many others – most particularly by the French chemist, Henry Sainte-Claire Deville, and his colleagues[43] – introduced into chemistry the concept of a reversible, thermally-dependent chemical equilibrium, and attempts to theoretically rationalize these equilibria led, in turn, to the first introduction of the kinetic-molecular theory into chemistry in 1867 by the Austrian chemist, Leopold Pfaundler,[44, 45] and to the first introduction of Clausius's entropy function into chemistry in 1873 by the German chemist, August Horstmann.[46, 47]

Application in the 1880s of the newer solution-phase methods for the determination of the molecular weights of solutes soon uncovered similar deviations from ideality. These were found to correlate with the electrical conductivity of the solutions in question and were soon interpreted as examples of dissociation into electrically conducting ions rather than neutral molecules:

$HCl(aq) \leftrightarrow H(aq)^+ + Cl(aq)^-$
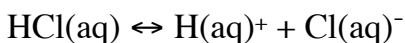
thus providing important supporting evidence for Arrhenius' newly proposed theory of ionic dissociation, as discussed in Booklet 8.

To accommodate this phenomena, van't Hoff introduced an empirical correction factor (*i*) into the various equations for the determination of molecular weights[33] which may be interpreted as the ratio of the ideal molecular weight (MW_{ideal}), as calculated from the formula of either the gas or dissolved solute, to that of its "apparent" molecular weight as determined experimentally (MW_{expt}):

$i = (MW_{ideal})/(MW_{expt})$ [19]

If $MW_{expt} = MW_{ideal}$, then $i = 1$ and the system obeys the ideal laws as written earlier. If $MW_{expt} < MW_{ideal}$, then $i > 1$ and the system has undergone some degree of

dissociation. Finally, if $MW_{expt} > MW_{ideal}$, then $i < 1$ and the system has instead undergone some degree of association. An early example of this latter phenomenon was the discovery that, in benzene solutions, carboxylic acids form dimers:[48]

$$2RCOOH \leftrightarrow (RCOOH)_2$$
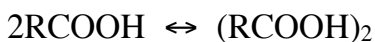
and the same process was later discovered in the gas phase as well, where over 56% of the molecules in acetic acid vapor are dimerized at temperatures just below its boiling point.[49] Attempts to theoretically rationalize this dimerization and related cases using G. N. Lewis's newly formulated electron-pair theory of chemical bond would provide evidence for the emerging concept of the hydrogen bond starting in the 1920s.[50]

Beginning around 1900, application of the classical methods for the determination of the molecular weights of solutes to natural biological materials, such as rubber, cellulose and various proteins, resulted not only in nonintegral values for x in equation 1 but in enormous values for the resulting molecular weights – often numbering in the tens or even the hundreds of thousands. Initially these were interpreted as yet another case of molecular association known as the *colloid* state. However, starting in the 1920s, the German chemist, Hermann Staudinger (figure 41), was able to present compelling evidence that many of these so-called colloidal clusters or micelles were actually gigantic macromolecules.[51, 52] Laboratory studies of synthetic macromolecules further showed that they usually consisted of mixtures of polymer chains of varying length so that the molecular weight values obtained using the classical methods were actually "average"

Figure 41. Hermann Staudinger (1881-1965).

molecular weights, thus accounting for the nonintegral x values.   .

As the study of both synthetic polymers and naturally occurring bio-macromolecules grew in importance throughout the 20th century, the relative importance of the various classical methods for molecular weight determination also began to change. The large polymer chains found in these materials seldom survived vaporization, so those classical methods based on gas and vapor densities proved worthless. The limited solubility of these materials and the extremely small changes in the temperatures of transition resulting from their enormous molecular weight values also limited the application of both the freezing-point depression and boiling-point elevation methods, not to mention the problem of possible denaturation of delicate biological materials induced by freezing or boiling their solutions.

The only classical method that was immune to these problems was the measurement of osmotic pressures which were of much greater magnitude than the corresponding changes in either freezing point or boiling point. Indeed, here the enormous molecular weights actually worked in its favor since the resulting reduction in the required counter pressures obviated many of the earlier problems with maintaining both high-pressure seals and the mechanical integrity of the membranes. In addition, several new approaches to the measurement of osmotic pressures soon appeared, including vapor pressure osmometry and the inhibition solvent movement across a membrane by applying negative hydraulic pressures to the solvent side rather than positive pressures to the solution side (figure 42).

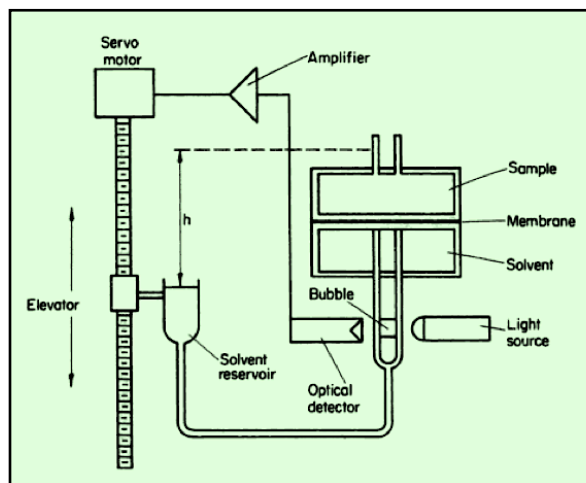In addition, Staudinger and other polymer chemists soon developed an

Figure 42. Schematic of the circa 1970 Mechrolab automated membrane osmometer. Movement of the solvent cross the membrane is detected by optically monitoring a solvent bubble and is automatically counteracted using a negative pressure created by raising or lowering the solvent reservoir.

Additional Methods
Isothermal Distillation
End Group Analysis
Static Light Scattering
Sedimentation Equilibrium
Sedimentation in a Density Gradient
Sedimentation Velocity/Diffusion
Solution Viscosity
Gel Permeation Chromatography

entire range of additional methods for molecular weight determinations for these materials based on correlations between the average molecular weights of various synthetic polymers and such physical properties as viscosity, light scattering, and sedimentation rates. Some of these are summarized in the adjacent table, though a detailed discussion of them is beyond the scope of this booklet.

Finally, in closing, a brief word should be said about why molecular weight determinations were of much greater importance to the 19th-century organic chemist than to the 19th-century inorganic chemist, though the definitive answer was not available until 1914 and the advent of X-ray diffraction methods for the determination of crystal structures. These quickly revealed that, in sharp contract to most organic solids, the vast majority (over 90%) of known inorganic solids do not contain discrete molecules but rather infinitely extended chain, layer and framework structures. As a consequence, when these materials are vaporized, they undergo molecular dissociation and, when they are dissolved, they either undergo ionic dissociation or solvolysis of some sort. In either case, the distinction between a relative formula and an absolute or molecular formula is meaningless for such materials.

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