While confining our present assessment to an index of accuracy, we have mentioned that the ROC is the proper basis for an evaluation of the usefulness of a diagnostic system, which would include elements of medical efficacy, risk, and cost. In such an evaluation one proceeds from probabilities of responses based on the diagnostic system under study, through a further decision-therapeutic tree, to health outcomes. The ROC is a means of determining the response probabilities appropriate to the best available estimates of the values, costs, and event probabilities that inhere in the relevant diagnostic and therapeutic context—and not merely the response probabilities associated with whatever decision criterion might have been employed in a test of the system (*13*). Costs and benefits may, therefore, be determined for a system operating at its best.

References and Notes

1. The materials and methods of this study are described in more detail, along with additional results and discussion, in *Technical Report No. 3818* from Bolt Beranek and Newman Inc., to the National Cancer Institute (1979).
2. W. W. Peterson *et al.*, *Trans. IRE Prof. Group Inf. Theory* **PGIT-4**, 171 (1954).
3. D. M. Green and J. A. Swets, *Signal Detection Theory and Psychophysics* (Wiley, New York, 1966; reprinted by Krieger, New York, 1974).
4. J. A. Swets, *Science* **182**, 990 (1973).
5. ——— and D. M. Green, in *Psychology: From Research to Practice*, H. L. Pick, Jr., H. W. Leibowitz, J. E. Singer, A. Steinschneider, H. W. Stevenson, Eds. (Plenum, New York, 1978), pp. 311-331.
6. L. B. Lusted, *Introduction to Medical Decision Making* (Thomas, Springfield, Ill., 1968); B. J. McNeil, B. Keeler, Jr., S. J. Adelstein, *N. Engl. J. Med.* **293**, 211 (1975); J. A. Swets, *Invest. Radiol.* **14** (No. 2), 109 (1979).
7. C. E. Metz, *Semin. Nucl. Med.* **8**, 283 (1978).
8. Principal investigators and institutions participating in the collaborative study were H. L. Baker, Jr., Mayo Clinic; D. O. Davis, George Washington University Medical Center; S. K. Hilal, Columbia University; P. F. J. New, Massachusetts General Hospital; and D. G. Potts, Cornell University Medical Center. Data coordination for the collaborative study was supplied by C. R. Buncher, University of Cincinnati Medical Center.
9. D. D. Dorfman and E. Alf, Jr., *J. Math. Psychol.* **6**, 487 (1969).
10. S. J. Starr, C. E. Metz, L. B. Lusted, D. J. Goodenough, *Radiology* **116**, 533 (1975).
11. M. G. Kendall, *Rank Correlation Methods* (Hafner, New York, 1962).
12. R. F. Jarrett and F. M. Henry, *J. Psychol.* **31**, 175 (1951).
13. J. A. Swets and J. B. Swets, in *Proceedings of the Joint American College of Radiology—IEEE Conference on Computers in Radiology* (IEEE Computer Society, Silver Spring, Md., in press).
14. Actively representing the sponsor to the project were R. Q. Blackwell, W. Pomerance, J. M. S. Prewitt, and B. Radovich. We are indebted to Dr. Prewitt for recognizing the need for a general protocol and for suggesting the present application. Members of an advisory panel, who contributed extensively to the protocol development and the design of this study, were S. J. Adelstein, H. L. Kundel, L. B. Lusted, B. J. McNeil, C. E. Metz, and J. E. K. Smith. J. A. Schnur participated throughout the project; consultants for the study reported here were W. B. Kaplan and G. M. Kleinman. We are indebted also to the principal investigators in the collaborative study (*8*). We thank the following radiologists, who participated as readers in the tests conducted at Bolt Beranek and Newman Inc.: computed tomography—L. R. Altemus, R. A. Baker, A. Duncan, D. Kido, J. Lin, and T. P. Naidrich; radionuclide scanning—H. L. Chandler, J. P. Clements, T. C. Hill, L. Malmud, F. D. Thomas, and D. E. Tow.

Molecular Thermodynamics for Chemical Process Design

The properties of fluid mixtures must be understood for economic manufacture of chemical products.

J. M. Prausnitz

Summary. Chemical process design requires quantitative information on the equilibrium properties of a variety of fluid mixtures. Since the experimental effort needed to provide this information is often prohibitive in cost and time, chemical engineers must utilize rational estimation techniques based on limited experimental data. The basis for such techniques is molecular thermodynamics, a synthesis of classical and statistical thermodynamics, molecular physics, and physical chemistry.

Chemical engineering design is concerned with finding economic and efficient methods for producing on a large scale what the chemist or materials scientist produces in small quantities. In meeting this concern, the chemical engineer must conceive, design, and build large units of equipment for processing large quantities of gases, liquids, and solids. Rational design of this equipment requires quantitative knowledge of the properties of the materials to be processed. Usually, these materials are mixtures.

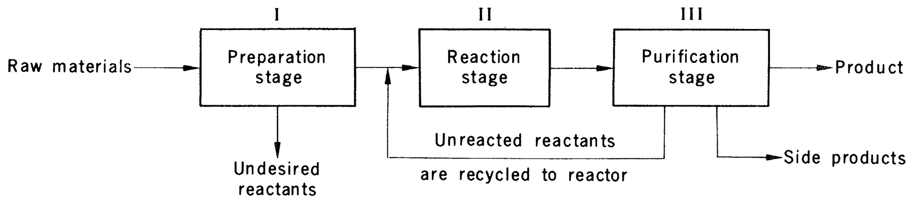
While test tubes and glass retorts are useful for manufacturing a few grams of a chemical substance, entirely different equipment is needed when manufacturing tons of that substance. Similarly, the chemical processes used for large-scale production are often highly dissimilar from those used for small-scale production. For example, a standard laboratory method for producing a few grams of hydrogen is to react hydrochloric acid with zinc, giving zinc chloride in addition to hydrogen. However, when hydrogen is needed in large amounts this procedure is inefficient, not only because the reactants are too expensive, but also because the available supply of zinc is too small to meet the world's need for hydrogen and because there would be a severe problem of what to do with vast amounts of zinc chloride. In principle, the zinc chloride could be reduced to recover zinc, but the expense of that operation would be prohibitive. For large-scale production of hydrogen, the traditional industrial method is to react steam with coal or other hydrocarbons or to oxidize partially natural gas with air.

In addition to dominant economic factors, there is a significant technical difference between laboratory-scale and industrial-scale production of typical chemical products. In the laboratory, the chemist generally uses pure reactants (for example, pure hydrochloric acid from one bottle and pure zinc from another) and the reaction is often so carried out that the desired product (gaseous hydrogen) and the undesired side product (solid zinc chloride) appear as separate phases, thereby avoiding any cumbersome separation operation. In industrial

---

The author is a professor in the Department of Chemical Engineering, University of California, Berkeley 94720.

0036-8075/79/0284-0759$01.75/0



Stages I and III require separation operations (such as distillation, absorption, extraction). In a typical chemical plant, 40-80% of investment is for separation-operation equipment.

Fig. 1. Schematic of a chemical plant.

processes, however, separations play a major role because more often than not the reactants as well as the products are mixtures, usually fluid mixtures.

The bulk raw materials that nature provides (such as petroleum and air) are rarely in pure form and therefore it is often necessary to separate desired from undesired reactants prior to chemical reaction and, similarly, to separate desired from undesired products after chemical reaction. Further, since a chemical reaction is rarely complete, it is usually necessary in addition to separate from the product stream the unreacted reactants, which are then recycled. Figure 1 illustrates schematically the need for separation operations in industrial chemical processes.

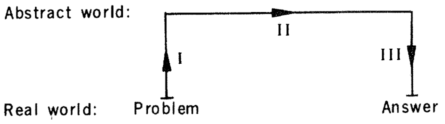
The heart of a chemical plant is the reactor, where reactants are converted to products. But in addition to a heart, a chemical plant also requires a mouth and a digestive system; purification (separation) operations are often necessary to prepare the reactants for reaction, and extensive purification is almost always necessary after the reactor to separate the products wanted from those that are not and from those reactants that have failed to react.

Separation of Mixtures

In typical cases, the various chemical species needed for reaction, as well as those leaving the reactor, are in the same phase (usually a gas or a liquid) and therefore separation can usually not be accomplished by a simple mechanical method such as filtration. Instead, it is necessary to establish separation by diffusional operations, such as distillation, absorption, and extraction. The costs associated with these operations often represent a substantial fraction of the total cost of the final product. In many chemical plants, the investment costs for separation operations account for 40 to 80 percent of the total; in some cases (for example, petroleum refineries), that percentage may be larger.

Design of chemical reactors depends strongly on the chemical properties of the reactants; that is, the properties that determine the tendency of the reactant molecules to react chemically to form new molecules. By contrast, design of separation operations depends strongly on the physical properties of the various molecules in the mixture, as on their relative volatilities in absorption or their relative solubilities in extraction. Efficient design of separation equipment therefore requires reliable techniques for estimating the physical properties of mixtures, not only to minimize the size and complexity of the equipment but also to minimize the energy requirement (heating, cooling, compressing, expanding) for operating it. This requirement has been of major importance for many years in the chemical (and related) industries, and it is becoming much more important now as energy is increasingly expensive and as convenient raw materials are increasingly scarce, to be replaced by other raw materials of lower grade. The chemical process industries therefore have a large financial incentive to find effective methods for determining the physical properties of mixtures to facilitate design of economic separation operations.

Considering the wide variety of mixtures that is encountered in chemical industry and the wide ranges of pressure, temperature, and composition that are met in chemical processes, it is not possible to measure experimentally all the physical properties needed for the design of efficient separation operations. It is desirable, indeed necessary, to establish generalizations for estimating physical properties of mixtures, using only limited experimental information. Molecular thermodynamics is an important tool for providing such generalizations.



Step I
Projection of real problem into an abstract (mathematical) formulation. (Definition of abstract quantities such as chemical potential.)

Step II
Solution of mathematical equations.

Step III
Reprojection of mathematical solution into physical reality. This is the hard step.

Fig. 2. Thermodynamics in practice: abstraction and reality.

Classical and Statistical Thermodynamics

Classical chemical thermodynamics, as developed more than 100 years ago by J. W. Gibbs, gives a comprehensive methodology for a broad description of the equilibrium properties of materials, including fluid mixtures. Gibbsian thermodynamics, because of its breadth and elegance, is one of the highlights of classical science, but at the same time it possesses severe limitations for practical work. Classical chemical thermodynamics gives a sweeping view, but it is not sufficient for quantitative results unless coupled with extensive—often prohibitive—experimental effort. The positive and negative features of classical thermodynamics are easily summarized:

1) Positive features: Broad, general description of nature. Applicable (in principle) to many phenomena. Rigorous mathematical formulation. Elegant, esthetically pleasing. Independent of any theory of matter.

2) Negative features: Uses abstract quantities, difficult to visualize. Interrelates experimental measurements but cannot predict a priori. Incomplete. For many practical applications need "metathermodynamics" (for example, physical models).

During the last 90 years, a vast literature on thermodynamics has accumulated. There are hundreds of textbooks and thousands of journal articles and every university offers several courses on various aspects of thermodynamics, thereby attesting to its academic respectability. Nevertheless, in practice, thermodynamics is often a disappointment to the chemical engineer. In textbooks, the reader finds dozens of equations wherein property A, which he seeks, is related to property B, which he does not know; property B is then related to property C and so on, until, at last, property Z is related to property A. To the nonexpert reader, texts on chemical thermodynamics seem to provide little more than a bureaucratic runaround. Unfortunately, classical thermodynamics never predicts any property by itself but only relates one property to another. The chemical engineer, seeking answers, often feels frustrated; thermodynamics has let him down. At the same time, many articles and compendiums tabulate large quantities of thermodynamic data, but more often than not, the published data do not apply to the practical problem of interest.

Classical thermodynamics is revered, honored, and admired, but in practice it is inadequate. The place of thermodynamics in relation to chemical engineering may be illustrated by two famous quotations about Helen of Troy: "Admired much, and much reviled" (Goethe, *Faust*, part II) and "Was this the face that launched a thousand ships?" (Marlowe, *Dr. Faustus*).

Application of abstract thermodynamics to real problems requires a three-step process, shown in Fig. 2. The real problem is first projected into an abstract mathematical world through the use of ingenious abstract functions (such as the chemical potential introduced by Gibbs) which, through the use of standard mathematical operations, allow the problem to be solved in the abstract world. The genius of classical thermodynamics lies in providing the abstract functions that enable elegant performance of steps I and II. The difficulty in reducing thermodynamics to practice lies in step III. In performing this last step, classical thermodynamics, by itself, is not sufficient. For step III, it is necessary to link abstract thermodynamic concepts with real physical properties.

Classical thermodynamics' independence of any particular theory of matter provides its glory, but this independence is also responsible for its weakness. In his later work, Gibbs tried to overcome this weakness through application of statistical physics as developed by Boltzmann, leading to statistical thermodynamics: an attempt to describe bulk (macroscopic) properties of matter in terms of (microscopic) intermolecular forces and the molecular structure of materials. Although statistical mechanics (the basis of statistical thermodynamics) has made remarkable progress since the early efforts of Gibbs and Boltzmann, it has not yet reached a stage where, by itself, it can yield practical methods for calculating the properties of real mixtures.

A candid view of statistical mechanics has been provided by Eugene Wigner, who said, "With thermodynamics, one can calculate almost everything crudely; with kinetic theory, one can calculate fewer things, but more accurately; and with statistical mechanics, one can calculate almost nothing, exactly." A chemical engineer is likely to be in full agreement with that view, except that he will be tempted to omit the word "almost."

$$P = kT\left[\frac{\partial \ln Q}{\partial V}\right]_{T,N}$$

N = No. of molecules
V = Total volume

For ideal gas:

$$Q = \frac{1}{N!}\left[\frac{V}{\Lambda^3}\right]^N\left[q_{r,v,e}\right]^N$$

$q_{r,v,e}$ = Molecular partition function for rotational, vibrational and electronic motions

$$\Lambda = \frac{h}{(2\pi mkT)^{1/2}}$$

h = Planck's constant
m = Molecular mass
k = Boltzmann's constant

Fig. 3. Equation of state from partition function *Q*.

Molecular Thermodynamics

Although statistical thermodynamics alone cannot provide the mixture properties needed for the design of separation operations, it does suggest techniques for constructing sensible physical models which, when coupled with appropriate concepts from molecular physics and physical chemistry, can be used to correlate limited experimental data. Such correlations can very much reduce the necessary experimental effort by providing good estimates of bulk properties through physically meaningful interpolation and extrapolation. These estimates are often sufficiently reliable for chemical process design.

Molecular thermodynamics is a synthesis of classical thermodynamics, statistical thermodynamics, molecular physics, and physical chemistry. It is an applied science in the sense that it combines, toward practical ends, the pertinent tools that physical science offers to the design engineer to help him solve important engineering problems. It is thus a compromise and a synthesis, as indicated by the following steps:

1) Use statistical thermodynamics whenever possible, at least as a point of departure.

2) Apply appropriate concepts from molecular physics and physical chemistry.

3) Construct physically grounded models for expressing (abstract) thermodynamic functions in terms of (real) measurable properties.

4) Obtain model parameters from very few, but representative, experiments.

In the next sections I present a few examples to illustrate how molecular thermodynamics provides quantitative estimates of mixture properties that are directly useful for chemical process design.

Applications of a Generalized van der Waals Partition Function

The first example indicates how an approximate partition function may be employed to obtain useful expressions for calculating phase equilibria typically encountered in the petroleum, natural gas, and polymer industries. To start, Fig. 3 reviews some well-known relations in

$$Q = \frac{1}{N!}\underset{①}{\left[\frac{V_f}{\Lambda^3}\right]^N}\underset{②}{\left[\exp - \frac{\phi}{2kT}\right]^N}\underset{③}{\left[q_{r,v,e}\right]^N}$$

V_f = Free volume
$\phi/2$ = Potential energy associated with one molecule

$$P = P^{(1)} + P^{(2)} + P^{(3)}$$

$$P^{(i)} = kT\left[\frac{\partial \ln[i]}{\partial V}\right]_{T,N} \qquad i = 1,2,3$$

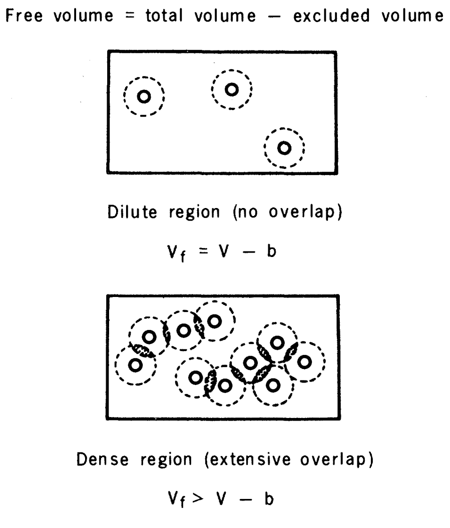


Fig. 4 (left). Basic assumptions of generalized van der Waals theory. Fig. 5 (right). Free volume V_f.

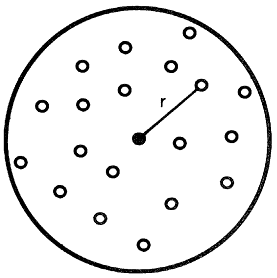
statistical thermodynamics. The partition function Q gives all thermodynamic properties through standard procedures: differentiation with respect to composition gives the chemical potential, differentiation with respect to temperature gives internal energy or entropy, and differentiation with respect to volume gives the equation of state. The last differentiation is of particular importance for molecular thermodynamics because it links the abstract partition function Q to directly measurable quantities: pressure P, volume V, and temperature T.

For an ideal gas it is simple to write an expression for Q, but for real fluids (gases and liquids) we can only write an approximate expression, following ideas that go back more than 100 years to van der Waals, as indicated in Fig. 4.

In an ideal gas, molecules are points that do not influence each other. However, molecules in a real fluid have a finite size, leading to repulsive forces at close molecule-molecule separations, and they have electronic configurations, leading to forces of attraction at intermediate separations. In the generalized van der Waals model, repulsive forces are taken into account through the concept of free volume V_f and attractive forces through the concept of a uniform potential field ϕ, as briefly explained below. But in addition to translational motions, molecules also have rotational and vibrational degrees of freedom, which contribute to the partition function. (Electronic degrees of freedom are important only at high temperatures and therefore are not of concern here.)

As shown in Fig. 4, there are three contributions to the equation of state. In recent years there has been much progress in understanding the first two contributions, but little is known about the third. Nearly all theoreticians who work in the area of fluids restrict attention to argon-like molecules where the third contribution disappears; the usual assumption is that for small, nearly spherical molecules, rotational and vibrational motions depend only on temperature and are independent of density. For larger molecules, especially those that are nonspherical, this simplifying assumption is not valid.

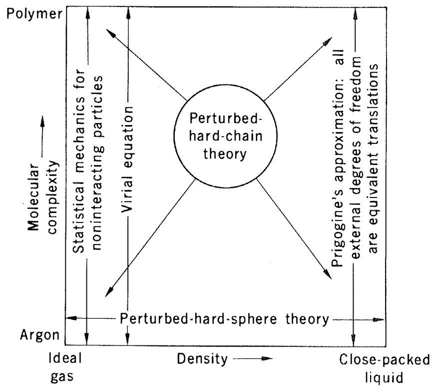
Figure 5 gives a two-dimensional view of the free-volume concept. The free volume is that part of the total volume which is accessible; because of the finite size of all molecules, a particular molecule, wandering about, does not have access to every part of the total volume since some of that volume (the excluded volume) is occupied by other molecules.



Potential energy between two molecules is $\Gamma(r)$.
Potential energy between central molecule and all others is

$$\phi = (N/V)\int_0^\infty \Gamma(r)g(r)\,4\pi r^2\,dr$$

$g(r)$ = Radial distribution function, tells where molecules are.



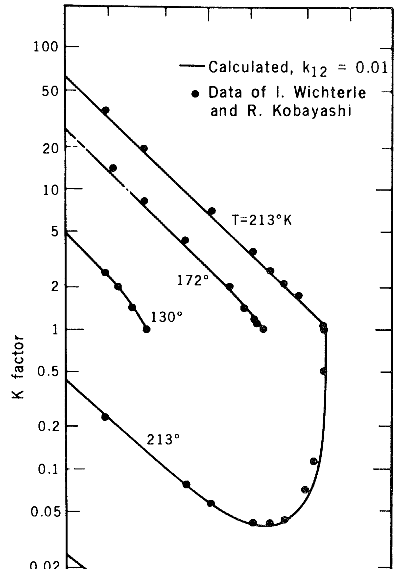


Fig. 6 (top). Potential energy ϕ. Fig. 7 (middle). Perturbed-hard-chain theory provides an equation of state for fluids containing simple or complex molecules, covering all fluid densities. Fig. 8 (bottom). K factors in the binary system methane-propane.

In Fig. 5, each molecule is represented by a billiard ball, or hard sphere. The finite size of a molecule is indicated by the dark line. Let one molecule approach another until the two surfaces are in contact; this is the closest possible molecule-molecule distance. The center of one of the molecules cannot penetrate the volume bounded by the dashed line around the other; that volume is not available: it is excluded. When the number of molecules is small (low density), this excluded volume is given by the van der Waals parameter b, which is proportional to the actual volume of all the finite-sized molecules.

At high densities, it is much more difficult to calculate the excluded volume because of overlap, as shown by the shaded areas in the lower part of Fig. 5. The excluded volume is less than the parameter b because in the calculation of b the overlapping regions are now erroneously counted more than once. Van der Waals and his co-workers were well aware of overlap but no satisfactory solution to this difficult mathematical problem was achieved until the middle 1960's. There is no need here to go into details; it is sufficient to say that for hard-sphere molecules we now have a reliable expression for the free volume, valid for all fluid densities (*1*, *2*).

Figure 6 gives a two-dimensional view of the uniform potential field concept. Consider the molecule at the center; we want to calculate the attractive-force field experienced by that molecule. The potential energy for any pair of molecules is designated by $\Gamma(r)$ where r is the center-to-center distance of separation. To sum up the contributions of all molecules interacting with the one at the center, we perform an integration, as shown. Imagine a sphere of radius r; the area of that sphere is $4\pi r^2$. We now build a thin shell on that area; the thickness of the shell is dr and its volume is $4\pi r^2 dr$. As a first estimate, we calculate the number of molecular centers in the shell by multiplying $4\pi r^2 dr$ by the overall density N/V. But that is a crude calculation which erroneously assumes that the local density (the density at position r) is always equal to the overall (or average) density. The structure of a fluid is not completely random; because of the finite size of the molecules, there is short-range order. When the magnitude of r is similar to that of the molecular diameter, the local density is very much different from the average density and therefore it is necessary to put into the integral some structural information given by the radial distribution function $g(r)$, which is the ratio of local density to average density. The notation $g(r)$ is deceptive; it erroneously implies that g is a function only of r, whereas in fact it is a strong function of density and, to a lesser extent, of temperature.

The last 20 years have produced significant progress in our understanding of the radial distribution function, especially because of the molecular dynamics studies of Alder *et al.* (*3*). Again, there is no need to go into details; it is sufficient to say that we now have useful theoretical methods for calculating ϕ as a function of density and temperature.

Large Molecules

For large molecules we must say something about the contributions from rotational and vibrational degrees of freedom or, more precisely, about the effect of volume on rotational and vibrational motions. To do so, contributions to the partition function from rotational and vibrational degrees of freedom are factored into an internal part (a function only of temperature) and an external part, which depends primarily on volume

$$Q = \frac{1}{N!}\left[\frac{V_f}{\Lambda^3}\right]^N \left[\exp\left(-\frac{\varphi}{2kT}\right)\right]^N [q_{\text{ext}}]^N [q_{\text{int}}]^N$$

where q_{int} is independent of density and therefore does not contribute to the equation of state.

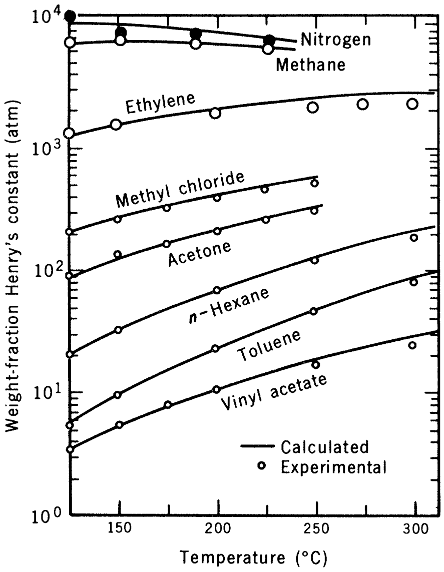
For the external part we assume a simple relation, suggested by Bazúa and Beret (*4*), which, in effect, is an interpolation between the known result at zero density and the high-density approximation of I. Prigogine, who assumed that those rotations and vibrations which are external (dependent on volume) can be treated as equivalent translations (*5*).

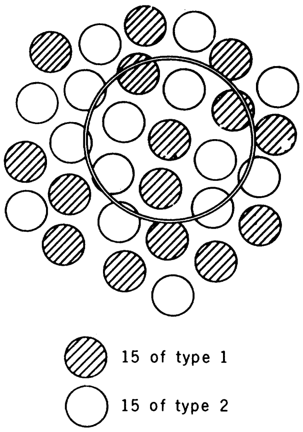
Bazúa and Beret suggest

$$q_{\text{ext}} = \left(\frac{V_f}{V}\right)^{c-1}$$

where $3c$ is the number of external (density-dependent) degrees of freedom: low-frequency, high-amplitude vibrations and rotations. For argon, $c = 1$. At liquid-like densitities, $V \approx$ constant. Then this partition function is the same as Prigogine's.

The domain of the resulting partition function, here called perturbed-hard-chain (PHC) theory, is shown in Fig. 7, where molecular complexity is one variable and density is the other. The PHC theory provides a smooth interpolation: At low densities, we have theoretical knowledge for simple and complex molecules; for simple molecules we have theoretical knowledge at all fluid densities (perturbed-hard-sphere theory); and at high densities, we have at least some theoretical knowledge if we adopt Prigogine's assumption. This theory is surely not rigorous, but it covers a wide region of practical interest by meeting the appropriate boundary conditions.





Overall mole fractions: $x_1 = x_2 = 1/2$

Local mole fractions:

$$x_{21} = \frac{\text{Molecules of 2 about a central molecule 1}}{\text{Total molecules about a central molecule 1}}$$

$x_{21} + x_{11} = 1$, as shown

$x_{12} + x_{22} = 1$

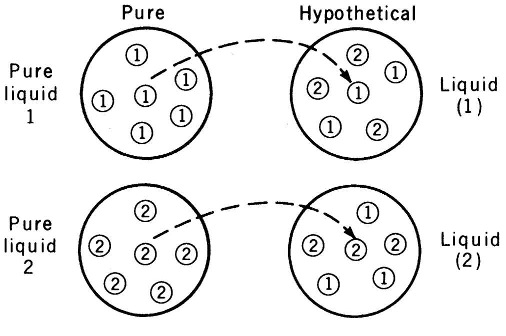
$x_{11} \sim 3/8$

$x_{21} \sim 5/8$

Fig. 9 (left). Weight-fraction Henry's constants in low-density polyethylene. Fig. 10 (right). Local compositions and the concept of local mole fractions.

The previous discussion has been confined to pure fluids but extension to mixtures is relatively simple through the one-fluid theory (*6*). This theory says that the thermodynamic properties of a fluid mixture are the same as those of a pure hypothetical fluid; the molecular parameters which characterize that hypothetical fluid are composition averages of the parameters which characterize the mixture's components.

Two examples illustrate possible applications of the PHC theory. First, Fig. 8 shows K factors for the binary mixture methane-propane, which is representative of mixtures found in a natural-gas technology. The K factor is a distribution coefficient, the ratio of the mole fraction in the vapor phase to that in the liquid phase. The top part of Fig. 8 (where $K > 1$) shows K factors for methane,



$$\boxed{U_{\text{mixture}} = x_1 U^{(1)} + x_2 U^{(2)}}$$

U = Internal energy

$U^{(1)} = x_{11}u_{11} + x_{21}u_{21}$

$U^{(2)} = x_{22}u_{22} + x_{12}u_{12}$

Gibbs-Helmholtz equation	Physical assumption
$A^E/T = \int_0^{1/T} \Delta U d(1/T)$	$x_{21}/x_{11} = x_2/x_1 \times \exp - (u_{21} - u_{11})/RT$
A^E = Excess free energy	$x_{12}/x_{22} = x_1/x_2 \times \exp - (u_{12} - u_{22})/RT$
T = Temperature	

Fig. 11. Local compositions and the two-liquid theory of mixtures.

while the lower part (where $K < 1$) shows K factors for propane, both plotted against pressure, up to the critical pressure where vapor and liquid are identical ($K = 1$ for every component). To make the indicated calculations, it was first necessary to reduce experimental pressure-volume-temperature (PVT) and vapor-pressure data for each of the pure components to obtain three characteristic molecular parameters: a hard-core size, a characteristic potential energy, and $3c$, the number of external degrees of freedom. (For methane, $c = 1$.) The mixing rules for applying one-fluid theory to the mixture contain only one adjustable binary parameter, designated by k_{12}, which gives the deviation from the geometric-mean assumption for calculating the characteristic potential energy for an unlike pair: $\epsilon_{12} = (\epsilon_{11}\epsilon_{22})^{1/2}(1 - k_{12})$. All parameters are independent of temperature, density, and composition. With only one adjustable binary parameter, PHC theory can represent the experimental mixture data for methane-propane over a wide range of conditions.

This first application is perhaps not very dramatic because there is only a modest difference in the molecular sizes of methane and propane. To indicate application to systems where the molecular size difference is large, Fig. 9 shows Henry's constants for several volatile solutes in polyethylene. As defined here, Henry's constant is the reciprocal of the solubility (weight fraction) when the partial pressure of the solute is 1 atmosphere. Again, the calculations require three molecular parameters for each pure component and one binary parameter. It is evident that PHC theory can represent a wide range of solubilities; note that the (logarithmic) scale on the ordinate covers five orders of magnitude. It is particularly gratifying that PHC theory can correctly reproduce the effect of temperature on solubility over an appreciable temperature range.

Phase equilibrium data, such as those shown in Fig. 9, are of particular importance in the design of a polymer devolatilization process wherein volatile, possibly toxic, solutes are removed from polymeric materials used for making clothing or food containers.

Strongly Nonideal Liquid Mixtures

Another application of molecular thermodynamics concerns strongly nonideal mixtures of liquids where orientational forces are appreciable; for example, mixtures of polar organic fluids, such as aldehydes, chlorinated hydrocarbons, ethers, nitriles, esters, and alcohols, including water. Such mixtures occur frequently in the petrochemical industry and, because of strong preferential interactions such as hydrogen bonding, it is not easily possible to describe such mixtures by a generalized van der Waals treatment coupled with the one-fluid theory of mixtures.

For liquid mixtures with strong orientational forces, we must take into account the tendency of molecules to segregate; that is, the existence of local order where molecules do not mix at random but instead show strong preferences in choosing their immediate neighbors. Although many outstanding scientists have tried to solve this difficult combinatorial problem, no satisfactory solution has been obtained for practical purposes. Therefore, it is necessary to construct an approximate model as suggested in Fig. 10, which introduces the concept of local composition.

The essential idea here is that, because of local order, the composition in a very small region of the solution is not the same as the overall composition. To illustrate, Fig. 10 shows 30 molecules, 15 shaded and 15 white; the overall mole fraction, therefore, is 1/2 for each component. We focus attention on one arbitrarily selected molecule of component 1 and describe the composition in the immediate vicinity of that molecule by two local mole fractions x_{11} and x_{21}; here x_{11} is the number of molecules of type 1 about the central molecule divided by the total number of molecules about that central molecule. An analogous definition holds for x_{21}, and there is the obvious conservation condition $x_{11} + x_{21} = 1$. As shown in Fig. 10, there are eight molecules about the central molecule; five are white and three are shaded. Therefore, the local compositions are $x_{11} = 3/8$ and $x_{21} = 5/8$.

The local-composition concept can be used as a point of departure to construct a simple expression for the nonideality of a liquid mixture, as shown in Fig. 11. The important feature is the boxed equation, which expresses a two-fluid theory of binary mixtures: the molar internal energy U is given by the mole-fraction average of $U^{(1)}$, the molar internal energy of hypothetical liquid (1), and $U^{(2)}$, the molar internal energy of hypothetical liquid (2). Hypothetical liquid (1) consists of a region in which molecule 1 is at the center and the local mole fractions are x_{11} and x_{21}; similarly, hypothetical liquid (2) consists of a region in which molecule 2 is at the center and the local mole fractions are x_{22} and x_{12}. Parameter u_{ij} characterizes the potential energy of an ij pair; where $i = 1$ or 2 and $j = 1$ or 2.

Given the relations shown, it is easily possible to derive an expression for ΔU, the energy change on mixing, in terms of the u_{ij} and the local mole fractions. This expression for ΔU is then substituted in-

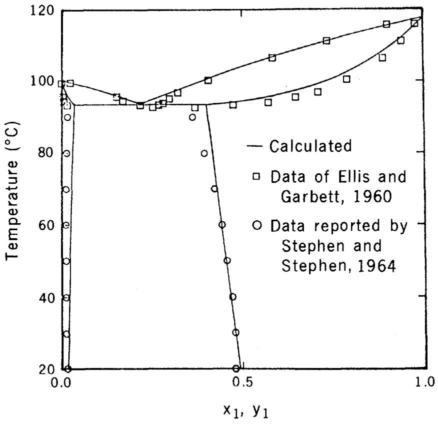


Fig. 12. Temperature-composition diagram for butanol (1)-water (2) system. Calculations are based on the UNIQUAC equation with temperature-independent parameters.

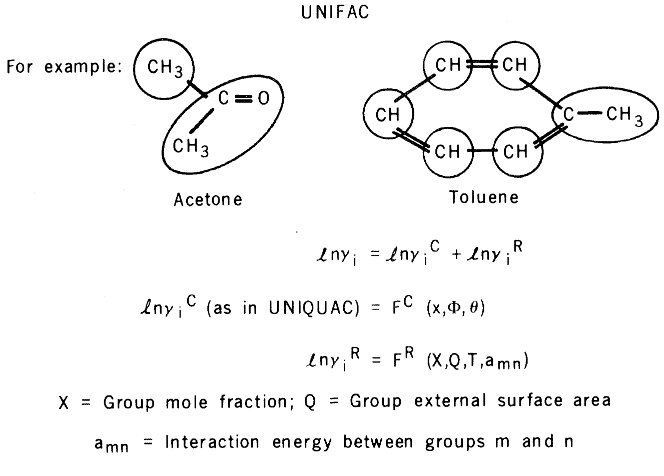


Fig. 13. Activity coefficient γ_i for molecular species i from group contributions. The configurational contribution F^c depends on (molecular) mole fraction x, site fraction Φ, and surface fraction θ. The residual contribution F^R depends on temperature and on group properties and group composition.

to the (classical) thermodynamic equation (shown at the lower left of Fig. 11) to obtain an expression for the excess Helmholtz energy, which in turn gives us the activity coefficients and thereby the deviations from ideality for the liquid mixture.

The remaining requirement is to say something useful about the local mole fractions, which are conceptual quantities and are not easily measured. To relate the local mole fractions to the measured overall mole fractions, we postulate a simple relation (shown at the lower right of Fig. 11) suggested by statistical mechanics: for each hypothetical liquid, the ratio of local mole fractions is assumed to be equal to the ratio of overall mole fractions, multiplied by a Boltzmann factor. This relation is in no sense rigorous, but it provides a reasonable approximation consistent with what statistical mechanics suggest about the properties of an assembly of molecules that differ appreciably in their intermolecular attractive forces.

Figure 11 illustrates the essential features of molecular thermodynamics of mixtures. At the lower left, we have classical thermodynamics; at the top, we have a physical model that attempts to reflect our limited knowledge of molecular behavior; and at the lower right, we have a relation suggested by statistical mechanics. Synthesis of these figures yields an expression for calculating mixture nonideality in terms of two adjustable parameters $u_{21} - u_{11}$ and $u_{12} - u_{22}$.

For simplicity, Figs. 10 and 11 represent only mixtures of equisized spherical molecules. However, the procedures outlined in Figs. 10 and 11 can be generalized to molecules of different size and shape by using local surface fractions (instead of local mole fractions), which are based on geometric properties of the molecules obtained from x-ray and similar data (*7*).

Figure 12 shows a temperature-composition diagram for a strongly nonideal mixture, *n*-butanol and water, based on the local-composition concept. By using only two adjustable parameters, it is possible to obtain an almost quantitative representation of the experimental data at a constant pressure of 1 atmosphere; at low temperatures, there are two liquid phases (partial miscibility) and at higher temperatures the vapor-liquid equilibria produce an azeotrope.

The phase diagram shown in Fig. 12 was calculated with a particular equation, called UNIQUAC for universal quasi-chemical (*8, 9*), based on the local-composition concept.

Activity Coefficients from Group Contributions

The local-composition concept is easily reconciled with an old idea (*10*) in applied thermodynamics: group contributions. The idea is that some thermodynamic properties of fluids containing polyatomic molecules can be calculated from interactions, not between the molecules, but between functional groups that constitute the molecules. This postulate can also be used for calculating activity coefficients, as shown in Fig. 13. In Fig. 13 an acetone molecule is divided into two functional groups and a toluene molecule into six functional groups of which five are identical. An extension of UNIQUAC yields simple expressions for activity coefficients in terms of surface fractions θ, site fractions Φ, and group-group interaction parameters a_{mn}, where m and n refer not to molecules, but to functional groups. This expression is called UNIFAC, an abbreviation for universal functional activity coefficient (*11, 12*). It is advantageous to use a group-contribution method for petrochemicals, in which the number of distinct functional groups is much smaller than the number of distinct molecules. Almost all petrochemicals, including polymers, can be constituted from perhaps 30 to 40 functional groups. If the interactions between these groups can be characterized, it is possible to estimate activity coefficients for a very large number of mixtures for which no experimental data have been obtained.

Group interaction parameters a_{mn} are calculated by data reduction for binary mixtures for which good experimental data are at hand. This has been done for a substantial number of group pairs. The UNIFAC equations are easily programmed for computer calculations, and the resulting equilibria for separation-process design. The accuracy of these estimates is not high but it is often sufficient for design purposes. Especially for preliminary calculations, UNIFAC provides a useful tool since it is applicable to a very large variety of mixtures for which no experimental information is available. It is not surprising that UNIFAC is popular with practicing chemical engineers, since it provides useful design data with little effort.

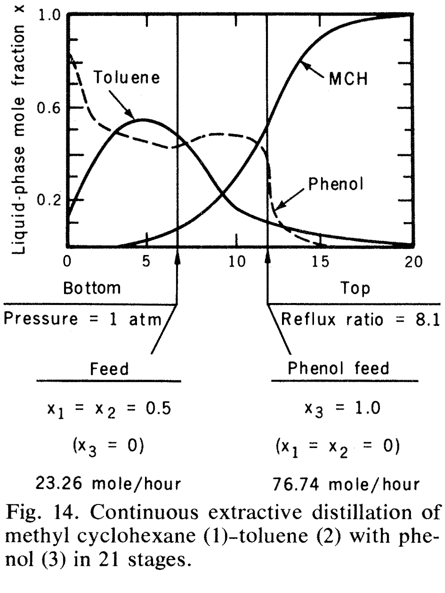


Fig. 14. Continuous extractive distillation of methyl cyclohexane (1)–toluene (2) with phenol (3) in 21 stages.

An engineering application of UNIFAC is shown in Fig. 14 which presents the composition profile of an extractive-distillation column. This equipment is used to separate a mixture of toluene and methyl cyclohexane (MCH). Since the boiling points of these liquids are close, ordinary distillation is difficult, requiring a large number of stages and hence a very tall (and expensive) distillation column. To facilitate separation, phenol is added to the liquid mixture because polar phenol depresses the volatility of (aromatic) toluene and raises the volatility of (saturated) MCH. Since an aromatic hydrocarbon has pi electrons and a saturated hydrocarbon does not, phenol "likes" toluene but "dislikes" MCH. Thus, phenol acts as an extractive agent, which in engineering language is called the entrainer. The presence of phenol drastically reduces the number of stages required for separation.

For proper design, it is necessary to calculate the equilibrium composition on each stage in the distillation column. The composition profile (Fig. 14) is calculated by using UNIFAC and material balances. Nearly pure MCH is obtained at the top of the column, while the bottom of the column yields a mixture of toluene and phenol, virtually free of MCH. The latter binary mixture must be separated in another distillation column, not shown here; however, that separation is simple, requiring only a few stages because the boiling point of phenol is much higher than that of toluene.

Conclusion

A few examples have been presented to illustrate the use of molecular thermodynamics to obtain a quantitative representation of mixture properties from a minimum of experimental data. These examples stress the important features of molecular thermodynamics. We start with the abstract concepts of thermodynamics, in particular the chemical potential, and then use whatever physical concepts we have to reduce abstract thermodynamics to reality.

Figure 2 shows the three-step thermodynamic process. The focus of molecular thermodynamics is on the last step: for useful results, the answer to the problem solved easily in the abstract world must be reprojected into the real world. To achieve this reprojection, we must go beyond classical thermodynamics, utilizing physical models based on molecular science.

In performing this reprojection step we must make compromises because rigorous procedures are hardly ever available for real situations. The last step requires some knowledge of appropriate physical concepts. But an even more important requirement is courage, willingness to make bold simplifying assumptions, to try them out and, if they fail, to choose some other simplifying assumptions and try again. Molecular thermodynamics is guided by Whitehead's famous advice to scientists: "Seek simplicity, but distrust it." But it is propelled forward by another, less well known sentence of Whitehead's: "Panic of error is the death of progress."

For chemical process design, molecular thermodynamics provides a useful tool for estimating, with a minimum of experimental effort, those equilibrium properties of mixtures which are required for efficient design of separation operations (for instance, distillation, extraction, and absorption). Since separation operations represent large investment and operating costs in the chemical and related industries, molecular thermodynamics contributes to the economic manufacture of chemical products.

References and Notes

1. N. F. Carnahan and K. E. Starling, *J. Chem. Phys.* **51**, 635 (1969).
2. C. A. Croxton, *Liquid State Physics—A Statistical Mechanical Introduction* (Cambridge Univ. Press, Cambridge, England, 1974), p. 73.
3. B. J. Alder, D. A. Young, M. A. Mark, *J. Chem. Phys.* **56**, 3013 (1972).
4. S. Beret and J. M. Prausnitz, *AIChE J.* **21**, 1123 (1975).
5. P. J. Flory, *Discuss. Faraday Soc.* **49**, 7 (1970).
6. M. D. Donohue and J. M. Prausnitz, *AIChE J.* **24**, 849 (1978).
7. A. Bondi, *Physical Properties of Molecular Crystals, Liquids and Glasses* (Wiley, New York, 1968).
8. G. Maurer and J. M. Prausnitz, *Fluid Phase Equilibria* **2**, 91 (1978).
9. T. F. Anderson and J. M. Prausnitz, *Ind. Eng. Chem. Process Des. Dev.* **17**, 526 (1978); *ibid.*, p. 551.
10. I. Langmuir, *Third Colloid Symposium Monograph* (Chemical Catalog Co., New York, 1925).
11. Aa. Fredenslund *et al.*, *Ind. Eng. Chem. Process Des. Dev.* **16**, 450 (1977).
12. Aa. Fredenslund, J. Gmehling, P. Rasmussen, *Vapor-Liquid Equilibria Using UNIFAC* (Elsevier, Amsterdam, 1977).
13. Supported by grants from the National Science Foundation, the Gas Processors' Association, the Gas Research Institute, and the Donors of the Petroleum Research Fund, administered by the American Chemical Society.

AAAS–Newcomb Cleveland Prize
To Be Awarded for an Article or a Report Published in *Science*

The AAAS-Newcomb Cleveland Prize is awarded annually to the author of an outstanding paper published in *Science* from August through July. This competition year starts with the 3 August 1979 issue of *Science* and ends with that of 25 July 1980. The value of the prize is $5000; the winner also receives a bronze medal.

Reports and Articles that include original research data, theories, or synthesis and are fundamental contributions to basic knowledge or technical achievements of far-reaching consequence are eligible for consideration for the prize. The paper must be a first-time publication of the author's own work. Reference to pertinent earlier work by the author may be included to give perspective.

Throughout the year, readers are invited to nominate papers appearing in the Reports or Articles sections. Nominations must be typed, and the following information provided: the title of the paper, issue in which it was published, author's name, and a brief statement of justification for nomination. Nominations should be submitted to AAAS-Newcomb Cleveland, Prize, AAAS, 1515 Massachusetts Avenue, NW, Washington, D.C. 20005. Final selection will rest with a panel of distinguished scientists appointed by the Board of Directors.

The award will be presented at a session of the annual meeting. In case of multiple authorship, the prize will be divided equally between or among the authors.