

the substrate with regions of the enzyme relatively distant from the catalytic site, with the virtually simultaneous formation or scission of several non-covalent bonds (multiple cooperative interaction). Evidence for this conclusion is available not only for pepsin and pepsin-like enzymes, but also for other proteinases, notably papain,³⁸ elastase,⁴³ and chymotrypsin.⁴⁴ Moreover, enzymes acting on oligosaccharides (lysozyme,⁴⁵ α -amylase⁴⁶) are known to have extended active sites. It is noteworthy that all these enzymes catalyze both hydrolytic reactions and transpeptidation or transglycosylation reactions⁴⁷ and it appears likely that secondary enzyme-substrate interactions may play a significant role in the catalytic mechanisms that are involved. In particular, transfer reactions such as $AB + HX \rightleftharpoons AX + BH$ require an ordered release of the A and B portions of AB, and significant differences in the energy of the interactions of A and B portions in a series of substrates for a given enzyme may have considerable effect on the kinetics of that enzyme. In the special case of pepsin, transpeptidation experiments have suggested that substrates such as Ac-Phe-Tyr are cleaved with the apparent prior release of the Ac-Phe portion and that the kinetic equivalent of an "imino-

(43) R. C. Thompson and E. R. Blout, *Biochemistry*, **12**, 57 (1973); D. Atlas and A. Berger, *ibid.*, **12**, 2573 (1973).

(44) W. K. Baumann, S. A. Bizzozero, and H. Dutler, *Eur. J. Biochem.*, **39**, 381 (1973).

(45) D. M. Chapman and N. Sharon, *Science*, **165**, 454 (1969).

(46) J. F. Robyt and D. French, *J. Biol. Chem.*, **245**, 3917 (1970).

(47) J. S. Fruton, *Harvey Lect.*, **51**, 64 (1957).

enzyme" (E-Tyr) can react with a suitable carboxylic acid to form RCO-Tyr. Several hypotheses have been offered^{8,9} to rationalize the transformation of the presumed tetrahedral intermediate I to an imino-enzyme, with the release of the acyl portion of the substrate. The status of these hypotheses is uncertain, however, since neither Ac-Phe-Tyr-NH₂ nor Ac-Phe-Phe-OEt gives transpeptidation products, raising doubt about the occurrence of a covalently bound E-Tyr intermediate.⁴⁸

Clearly, the further study of the mechanism of pepsin action requires closer study with substrates of the type A-Phe-Phe-OP₄P and Phe-Gly-His-Phe(NO₂)-Phe-B, where the A and B groups contain amino acid units that enhance the catalytic efficiency of the enzyme. Moreover, an examination of the action of pepsin on comparable ester substrates, where the sensitive Phe-Phe unit has been replaced by Phe-Pla, is needed. It will be of interest to compare the results with those for carboxypeptidase A, whose mechanism appears to resemble that of pepsin in several respects.⁴⁹

The research of our laboratory reported in this article was aided by grants from the National Institutes of Health (GM-18172 and AM-15682) and from the National Science Foundation (GB-37871). I also thank Professor Lubert Stryer for many helpful discussions and for his valuable comments on an early draft of this article.

(48) M. S. Silver and M. Stoddard, *Biochemistry*, **11**, 191 (1973).

(49) E. T. Kaiser and B. L. Kaiser, *Accounts Chem. Res.*, **5**, 219 (1972).

Equilibrium Structure and Molecular Motion in Liquids

David Chandler

School of Chemical Sciences, University of Illinois, Urbana, Illinois 61801

Received March 27, 1974

Much progress has been made recently in the theory of liquids.¹ The principal physical concept associated with this progress originated with the work of van der Waals long ago. It is the idea that, for a dense fluid, the repulsive forces (which are nearly hard-core interactions) dominate the liquid structure. This means that the *shape* of molecules determines the intermolecular correlations. Attractive forces, dipole-dipole interactions, and other slowly varying forces play a minor role. As a result, if a dense liquid is composed of spherical (or nearly spherical) molecules, the intermolecular structure should be very similar to that of a fluid made up of hard spheres.

Professor Chandler's research interests include microscopic theory of the static and dynamic structure of simple and molecular liquids, ionic solutions, and phase transitions. He was born in Brooklyn in 1944. He received the B.S. degree from Massachusetts Institute of Technology and the Ph.D. from Harvard University (in 1969), after which he spent a postdoctoral year at University of California, San Diego. Since 1970 he has been on the faculty of the University of Illinois at Urbana-Champaign. He is an Alfred P. Sloan Foundation Research Fellow.

Most of the modern theories of liquids have focussed attention on this concept, and calculations have shown that the idea is quantitatively accurate for many liquids.¹⁻⁹ Further, it has been shown by Longuet-Higgins and Widom⁷ and by others¹⁰ that liquids freeze when the density becomes high enough that *steric effects* (not attractive forces) lock the molecules into a structure for which particle diffu-

(1) For a recent review, see J. A. Barker and D. Henderson, *Annu. Rev. Phys. Chem.*, **23**, 439 (1972).

(2) D. Chandler and J. D. Weeks, *Phys. Rev. Lett.*, **25**, 149 (1970).

(3) J. D. Weeks, D. Chandler, and H. C. Andersen, *J. Chem. Phys.*, **54**, 5237 (1971); **55**, 5421 (1971).

(4) H. C. Andersen, J. D. Weeks, and D. Chandler, *Phys. Rev. A*, **4**, 1597 (1971).

(5) L. Verlet and J.-J. Weis, *Phys. Rev. A*, **5**, 939 (1972).

(6) J. A. Barker and D. Henderson, *Phys. Rev. A*, **4**, 806 (1971).

(7) H. C. Longuet-Higgins and B. Widom, *Mol. Phys.*, **8**, 549 (1964); B. Widom, *Science*, **157**, 375 (1967).

(8) J. A. Barker and D. Henderson, *Accounts Chem. Res.*, **4**, 303 (1971); J. A. Barker and D. Henderson, *J. Chem. Phys.*, **47**, 4714 (1967).

(9) L. Verlet and J.-J. Weis, *Mol. Phys.*, **24**, 1013 (1972).

(10) J. P. Hansen and L. Verlet, *Phys. Rev.*, **184**, 151 (1969); D. Henderson and J. A. Barker, *Mol. Phys.*, **14**, 587 (1968); J.-J. Weis, preprint; R. K. Crawford, *J. Chem. Phys.*, **60**, 2169 (1974).

sion is nearly impossible. For systems composed of spherical molecules, the liquid–solid phase transition is intimately related to the fluid–solid transition observed by computer simulations on hard-sphere systems.¹¹ Thus, a child playing with a box of marbles has witnessed the microscopic structure of dense liquids and the mechanism for freezing.

The only important exceptions to this idea seem to be liquid water, a few highly polar liquids (in particular, HCl and HF), ionic solutions, and fused salts. The theory discussed in this article cannot, in any straightforward way, be used to describe these exceptions.

A qualitative explanation for why the repulsive intermolecular forces dominate the structure of most dense fluids follows from a description of the environment of a particle in a liquid. For simplicity, consider an atomic liquid. The phase diagram is shown in Figure 1. High density corresponds to thermodynamic states at which $\rho^{-1/3} \lesssim r_0$, where ρ is the average number of particles per unit volume, and r_0 is the location of the minimum in the intermolecular pair potential. A glance at the phase diagram shows that “high density” characterizes most of the liquid phase outside of the critical region. Note that $\rho^{-1/3}$ provides an estimate of the average separation between nearest neighbors. Thus, in a dense liquid, nearest neighbors are crushed extremely close to one another. Any displacement of a particle will cause a large change in the energy associated with the interparticle repulsive forces. The change in energy associated with the attractive forces will be relatively small because these interactions are not quickly varying functions of the interparticle separation. As a result, the repulsions dominate the high-density structure. (Notice that, if the attractions were quickly varying, they would play an important role in the liquid structure. This is the reason for each of the exceptions listed above. For example, the hydrogen bond interactions in water are as quickly varying as most of the repulsive forces in that liquid.¹²)

To demonstrate quantitatively the dominance of repulsive forces on the liquid structure, we first consider a specific system. It is shown that the pair correlation function for the Lennard-Jones fluid (a model for atomic liquids) is indeed determined mainly by the repulsive portions of the intermolecular interactions. The relevance of this work to understanding the structure of molecular fluids is discussed also. Then we consider molecular motion in liquids. In particular, the diffusion constant and the velocity autocorrelation function for atomic liquids are investigated. It is seen, once again, that steric effects dominate the nature of particle motion in dense fluids. Finally, rotational motion in molecular liquids is discussed.

Static Structure of Liquids

To make the discussion of the liquid structure quantitative, we consider in this section a simple but precise and revealing model system: the Lennard-Jones liquid. This is the classical fluid in which the interparticle potentials are the 6–12 pair interac-

(11) W. G. Hoover and F. H. Ree, *J. Chem. Phys.*, **49**, 3609 (1968), and references cited therein.

(12) R. A. Horne, Ed., “Water and Aqueous Solutions,” Wiley-Interscience, New York, N. Y., 1972.

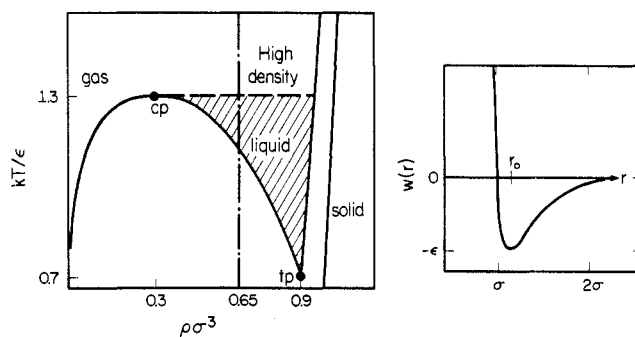


Figure 1. Phase diagram (left) and intermolecular pair potential (right) for the Lennard-Jones fluid. For particular choices of the length and energy parameters, σ and ϵ , the Lennard-Jones system is a qualitatively accurate model for several liquids (see ref 9). Notice that the density at the critical point (cp) is roughly one-third the density at the triple point (tp) and the critical temperature is about twice the triple temperature. This approximate scaling holds for nearly all nonhydrogen-bonding liquids that are composed of molecules that are relatively small (having $\lesssim 10$ atoms). Thus, the phase diagram shown here is a qualitative representation of the phase diagram for many one-component fluids. The “high density” region comprises thermodynamic states for which the particle density, ρ , is greater than about twice the critical density, ρ_c .

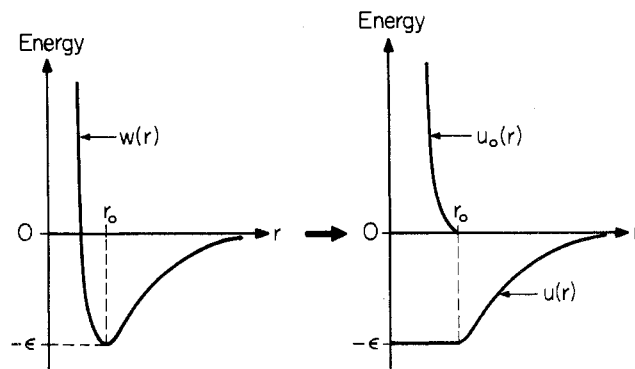


Figure 2. The unique separation of the Lennard-Jones potential, $w(r)$, into a part $u_0(r)$ containing all the repulsive interactions in $w(r)$ (and no attractions) and a part $u(r)$ containing all the attractive interactions in $w(r)$ (and no repulsions). See ref 2 and 3.

tions: $w(r) = 4\epsilon[(\sigma/r)^{12} - (\sigma/r)^6]$. Here, r denotes the separation between a pair of particles, and ϵ and σ are constants with units of energy and length, respectively. With the appropriate choices of ϵ and σ , the Lennard-Jones liquid is a qualitative model for liquid argon. However, the usefulness of the model for our purposes rests on the fact that the properties of the system are known from the results of computer simulations.^{13–15} These “exact” machine calculations provide us with “experimental” data on a system for which the intermolecular interaction is unambiguously known. The interaction, $w(r)$, contains both repulsive and attractive forces. Let $u_0(r)$ and $u(r)$ denote the repulsive and attractive portions, respectively. The decomposition of $w(r)$ into these two parts is shown in Figure 2.

(13) Thermodynamic properties obtained by molecular dynamics computations on the Lennard-Jones fluid are tabulated by L. Verlet, *Phys. Rev.*, **159**, 98 (1967). Monte Carlo calculations are reported by D. Levesque and L. Verlet, *Phys. Rev.*, **182**, 307 (1969), and by J.-P. Hansen and L. Verlet.⁹

(14) Molecular dynamics calculations on the equilibrium structure of the Lennard-Jones fluid are reported by L. Verlet, *Phys. Rev.*, **165**, 201 (1968).

(15) Molecular dynamics studies of the dynamic properties of the Lennard-Jones liquid are reported by A. Rahman, *Phys. Rev.*, **136**, A405 (1964); D. Levesque and L. Verlet, *Phys. Rev. A*, **2**, 2514 (1970); D. Levesque, L. Verlet, and J. Kurkijarvi, *Phys. Rev. A*, **7**, 1690 (1973).

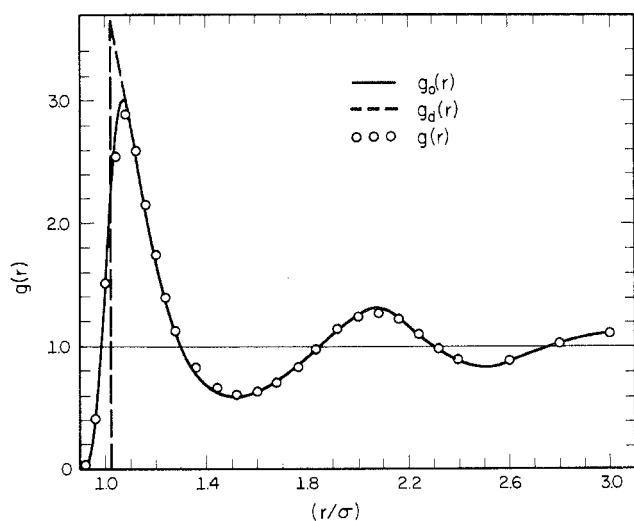


Figure 3. The radial distribution function for the Lennard-Jones liquid, $g(r)$, as determined from computer simulations¹⁴ compared with the radial distribution functions due to the repulsive forces, $g_0(r)$, and the associated hard-sphere interactions, $g_d(r)$. The thermodynamic state is $k_B T/\epsilon = 0.88$ and $\rho\sigma^3 = 0.85$.

The structure of atomic liquids, and of the Lennard-Jones fluid in particular, is described quantitatively by the *radial distribution function*, $g(r)$. This is defined so that $4\pi\rho r^2 g(r)$ is the probability distribution for finding a particle a distance r from the origin, given that another particle is at the origin. Computer simulations have been used to determine $g(r)$ for the Lennard-Jones liquid.¹⁴

To see how the repulsive interaction, $u_0(r)$, contributes to $g(r)$, one considers the hypothetical fluid for which the total pair interaction is $u_0(r)$, so that there are no attractive intermolecular forces. The radial distribution function for the system, $g_0(r)$, can be calculated and compared with the experimental Lennard-Jones $g(r)$. Calculations of $g_0(r)$ have been done both by an analytic theory²⁻⁴ and by computer simulations on the repulsive force system.^{5,6} The comparison between $g(r)$ and $g_0(r)$ is shown in Figure 3 for a thermodynamic state close to the triple point. The temperature is very low. Thus, the remarkably close agreement between $g(r)$ and $g_0(r)$ is not a trivial consequence of having $u(r)$ small compared to $k_B T$ (k_B stands for the Boltzmann constant and T is the temperature). Rather, the agreement is a manifestation of the high density. Particles are so close together that steric effects form the interparticle correlations.

Since the repulsive pair interaction, $u_0(r)$, is very harsh, it seems reasonable that the properties of the repulsive force system should be closely related to those of an appropriately chosen hard-sphere system. Indeed, it has been shown⁴ that there is an optimum hard-sphere diameter d which defines the hard-sphere fluid that is most closely associated with the repulsive force system. The radial distribution function for this associated hard-sphere system, $g_d(r)$, is also shown in Figure 3. Notice that, except for a small range of r values, $g_d(r)$ and $g_0(r)$ are identical. The correspondence between the hard-sphere fluid and fluids with realistic repulsive forces⁴ is exploited in the analytic theory for $g_0(r)$.^{3,4} For each thermodynamic state, the optimum d value is somewhat different. The qualitative behavior of the optimum d can be sum-

marized as follows: (a) $d < r_0$; (b) the diameter decreases with increasing temperature (this is easily understood since the average kinetic energy increases with temperature, and as a result the average classical turning point for $u_0(r)$ decreases with increasing temperature); and (c) the diameter decreases with increasing density (though this effect is much smaller than the temperature dependence of d).

The results presented above demonstrate that at high densities the structure of the Lennard-Jones liquid is indeed dominated by the repulsive portion of the intermolecular potential. Further, the structure is essentially the same as that in the optimum hard-sphere fluid. There is an obvious logical consequence of these facts when considering more complicated systems: the structure of a molecular liquid is determined by the shape of the molecules which comprise the fluid. Thus, for example, the arrangement of molecules in a liquid crystal composed of long molecules is correctly understood in terms of the packing of long hard particles. It is *not* understood by imagining that the structure is formed by dipole-dipole interactions.

The ideas emphasized above concerning the equilibrium structure of liquids can also be used to study thermodynamic properties. This approach leads to a first-order "thermodynamic perturbation theory"¹⁶ for the Helmholtz free energy that is very accurate.³ The theoretically inclined reader may be happy to know that a rigorous many-body theory, called the optimized cluster expansions, has been developed to describe the role of *attractive* forces in liquids.¹⁷ The theory provides a quantitative explanation for how the repulsive forces screen the effects of attractions at high densities. Further, it gives an accurate theory for fluids at low and moderate densities.¹⁸⁻²⁰ Finally, the ideas discussed above have been used to make explicit calculations on realistic models for fluids composed of nonspherical molecules.²¹

Molecular Motion in Simple Liquids

We have shown in the previous section that the structures of liquids composed of nearly spherical molecules is similar to that of a hard-sphere fluid. As a result, it is reasonable to suppose that the dynamics—molecular motion—occurring in many liquids is similar to that in a hard-sphere fluid. This idea was probably first exploited by Enskog.²² In more modern times it has guided the work of many others.²³ In this and the following section we review a theory of molecular motion in liquids which is based on the same idea.²⁴⁻²⁶

(16) L. Landau and E. M. Lifshitz, "Statistical Physics," Pergamon Press, London, 1958, Section 32.

(17) H. C. Andersen and D. Chandler, *J. Chem. Phys.*, **57**, 1918 (1972).

(18) H. C. Andersen, D. Chandler, and J. D. Weeks, *J. Chem. Phys.*, **57**, 2626 (1972).

(19) S. H. Sung and D. Chandler, *Phys. Rev. A*, **9**, 1688 (1974).

(20) S. H. Sung, D. Chandler, and B. J. Alder, *J. Chem. Phys.*, in press.

(21) S. H. Sung and D. Chandler, *J. Chem. Phys.*, **56**, 4989 (1972); L. Lowden and D. Chandler, *J. Chem. Phys.*, **59**, 6587 (1973).

(22) See Chapter 16 of S. Chapman and T. G. Cowling, "Mathematical Theory of Non-Uniform Gases," 3rd ed, Cambridge University Press, Cambridge, England, 1970.

(23) The list of publications along these lines is huge. Some representative references are: S. A. Rice and P. Gray, "Statistical Mechanics of Simple Liquids," Interscience, New York, N. Y., 1965; P. Protopapas, H. C. Andersen, and N. A. D. Parlee, *J. Chem. Phys.*, **59**, 15 (1973); R. G. Gordon, R. L. Armstrong, and E. Tward, *J. Chem. Phys.*, **48**, 2655 (1968). Also see the work of Verlet and coworkers.¹⁵

Molecular motions in equilibrium fluids are conveniently characterized by time correlation functions of the form $\langle AB(t) \rangle$.²⁷⁻²⁹ Here, $A(t)$ and $B(t)$ denote dynamical variables which depend on time, t , through the time dependence of the coordinates and momenta of the molecules in the system; $A = A(0)$; and the pointed brackets denote the equilibrium ensemble average over initial conditions (*i.e.*, the coordinates and momenta at $t = 0$). Interest in these correlation functions has grown due to the recognition that time correlation functions are actually measured quantities when one performs various spectroscopic experiments.²⁷⁻²⁹

The simplest of these time correlation functions is the velocity autocorrelation function which is defined as

$$C_v(t) = \langle \mathbf{v} \cdot \mathbf{v}(t) \rangle / \langle v^2 \rangle \quad (1)$$

where \mathbf{v} denotes the center of mass velocity of a "tagged" molecule in the liquid. The self-diffusion constant, D , is related to the zero frequency part of the velocity autocorrelation function by the familiar equation

$$D = (k_B T/m) \int_0^\infty C_v(t) dt \quad (2)$$

where m stands for the mass of the molecule. In principle, $C_v(t)$ can be measured by neutron scattering experiments performed on a liquid.²⁹ However, this has never been done, and our only experimental knowledge concerning $C_v(t)$ stems from computer simulations.^{15,30}

The computer simulations have established the following facts.

(1) At high densities ($\rho > 2\rho_c$), the diffusion constant for the Lennard-Jones fluid, D_{LJ} , and the diffusion constant of the associated hard-sphere fluid, D_d (d stands for the optimum hard sphere diameter discussed earlier), are nearly the same

$$D_{LJ} \approx D_d \quad (3)$$

where the error in eq 3 is $\lesssim 10\%$.

(2) The velocity autocorrelation function for the hard-sphere fluid $[C_v(t)]_d$ is given to qualitative accuracy by the Enskog formula

$$[C_v(t)]_d \approx e^{-t/\tau_E} \quad (4)$$

where $\tau_E = [(8/3)(\pi k_B T/m)^{1/2} \rho d^2 g_d(d)]^{-1}$ is the Enskog relaxation time. Equation 4 is exact at small times. It incurs errors for times greater than τ_E , but the magnitude of the absolute error in eq 4 is always less than 0.03. Thus, for hard spheres, the velocity autocorrelation function looks very much like an exponential.

(3) The velocity autocorrelation function for the Lennard-Jones fluid, $[C_v(t)]_{LJ}$, does *not* look anything like an exponential. In fact, at densities near

the triple point, $[C_v(t)]_{LJ}$ has a *negative* peak with a magnitude of the order of 0.2. At such high densities, the hard-sphere correlation function is also negative for a period of time. But the magnitude of the negative peak in $[C_v(t)]_d$ is about 0.02, an order of magnitude less than that in the Lennard-Jones correlation function.

The first fact listed above seems to be in agreement with the point of view emphasized in the preceding sections (though now we are discussing dynamics and not the static structure of liquids), but the second and third facts indicate that the velocity autocorrelation function for hard spheres is very different than that for a realistic liquid. One might think that the difference is a manifestation of the attractive forces which are present in the Lennard-Jones fluid and are obviously absent in the hard-sphere system. If this were correct, then the attractions would play a significant role in the dynamics occurring in liquids. However, we will see below that the differences are actually due to the duration time of *repulsive* force collisions. To an excellent approximation, the attractive interactions may be neglected when discussing the dynamic structure as well as the static structure of liquids.

To analyze the differences between the velocity autocorrelation functions for the Lennard-Jones and hard-sphere fluids, it is convenient to introduce the memory function which is defined in terms of the reciprocal of the Laplace transform of the correlation function³¹

$$s + \tilde{M}_v(s) = 1/\tilde{C}_v(s) \quad (5)$$

where s is the Laplace transform variable, $\tilde{M}_v(s)$ is the Laplace transform of the memory function $\tilde{M}_v(t)$, and $\tilde{C}_v(s)$ is the Laplace transform of $C_v(t)$.

The Enskog theory for $[C_v(t)]_d$, namely eq 4, is equivalent to writing $[\tilde{M}_v(s)]_d \approx \tau_E^{-1}$, which implies

$$[M_v(t)]_d \approx 2\tau_E^{-1}\delta(t) \quad (6)$$

From the binary collision expansion³² it can be shown that eq 6 is obtained by including in the memory function a binary collision between a single pair of particles that are initially nearest neighbors. In this case, $[M_v(t)]_d$ is a δ function because hard-sphere binary collisions are impulsive—they occur with a duration time of zero. All other dynamical events which in principle contribute to the memory function are neglected. This, it can be shown, means that the Enskog theory for $[C_v(t)]_d$ approximates the dynamic processes contributing to the correlation function by sequences of *uncorrelated* nearest neighbor binary collisions. Since the Enskog theory is fairly accurate, this approximation to the dynamics must be qualitatively correct.

Let us assume the same approximation is reliable when considering particle motion in the hypothetical fluid for which the pair interaction is $u_0(r)$ (*i.e.*, the repulsive part of the Lennard-Jones potential). This seems reasonable since $u_0(r)$ is a harsh repulsion. However, $u_0(r)$ is smooth and, as a result, binary col-

(24) K. Kim and D. Chandler, *J. Chem. Phys.*, **59**, 5215 (1973).

(25) D. Chandler, *J. Chem. Phys.*, **60**, 3500 (1974).

(26) D. Chandler, *J. Chem. Phys.*, **60**, 3508 (1974).

(27) R. Zwanzig, *Annu. Rev. Phys. Chem.*, **16**, 67 (1965).

(28) R. G. Gordon, *Advan. Magn. Resonance*, **3**, 1 (1968).

(29) P. C. Martin, "Measurements and Correlation Functions," Gordon and Breach, New York, N. Y., 1968.

(30) Molecular dynamics studies of the velocity autocorrelation function for the hard sphere fluid are reported by B. J. Alder and T. E. Wainwright, *Phys. Rev. Lett.*, **18**, 988 (1967).

(31) H. Mori, *Progr. Theoret. Phys.*, **33**, 423 (1965); B. J. Berne in "Physical Chemistry: An Advanced Treatise," Vol. VIII B, D. Henderson, Ed., Academic Press, New York, N. Y., 1971. Also see P. C. Martin.²⁹

(32) R. Zwanzig, *Phys. Rev.*, **129**, 486 (1963).

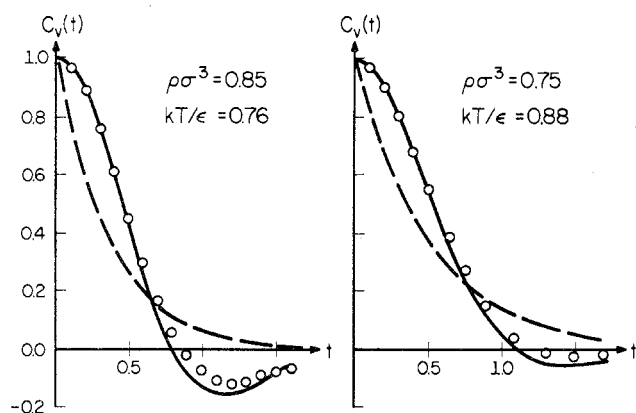


Figure 4. The velocity autocorrelation function for the Lennard-Jones liquid at two representative states. The solid line represents the repulsive force correlation function, $[C_v(t)]_0$, calculated with the methods described in the text. The dashed line is the Enskog hard-sphere correlation function. The circles denote the molecular dynamics results for the Lennard-Jones correlation function.¹⁵ The units of time are t_0 defined by Verlet and coworkers.¹⁵ For argon, $t_0 \approx 3 \times 10^{-13}$ sec.

collisions associated with it occur for a finite period of time. Thus, the Enskog theory must be generalized to account for the finite duration time of collisions. We do this approximately by assuming that the memory function for the repulsive force system can be written as a δ -like function with a finite width. When the duration times goes to zero (imagine changing $u_0(r)$ continuously to the hard-sphere potential), the width must vanish so that $[M_v(t)]_0$ becomes the hard-sphere δ function. Hence, a reasonable form for $[M_v(t)]_0$ is

$$[M_v(t)]_0 \approx A e^{-Bt^2} \quad (7)$$

To determine the constants A and B , two conditions must be imposed. First, we require that the approximate formula for $[M_v(t)]_0$ gives the exact value at $t = 0$. This produces²⁹

$$A = (\rho/3m) \int g_0(r) \nabla^2 u_0(r) \mathbf{d}\mathbf{r} \quad (8)$$

Next, we require that

$$\int_0^\infty [M_v(t)]_0 dt = \int_0^\infty [M_v(t)]_d dt \quad (9)$$

which means that we are equating the zero frequency responses (and thus the diffusion constants) of the hard-sphere and repulsive force fluids. A mathematical justification for eq 9 can be derived.²⁵ Physically, however, the condition is very reasonable. It simply means that, when we coarse-grain in time (the zero frequency limit), the hard-sphere and repulsive force systems are indistinguishable. Within the accuracy of eq 6 and 7, eq 9 is

$$(A/2)(\pi/B)^{1/2} = \tau_E^{-1} \quad (10)$$

In the limit that $u_0(r)$ becomes the hard-sphere potential, A diverges since the integral in eq 8 becomes infinite, and B diverges in a way which keeps $A/B^{1/2}$ finite. Thus, in that limit, eq 7 reduces to the Enskog formula, eq 6.

Equations 7, 8, and 10 provide a simple theory for the velocity autocorrelation function of a repulsive force system.²⁴ It is a phenomenological generalization of Enskog theory. The generalization is analo-

gous to the rigorous method used in ref 2-4 to relate the static correlation functions $g_0(r)$ and $g_d(r)$. Since the basis of the theory is the Enskog formula, the results obtained from the theory should be qualitatively accurate (*i.e.*, we do not expect absolute errors in $[C_v(t)]_0$ that are larger than 0.03). In Figure 4, the repulsive force correlation function, $[C_v(t)]_0$, obtained from eq 7, 8 and 9 is compared with the Lennard-Jones correlation function and the Enskog hard-sphere function at two representative high density states. It is seen that the dramatic differences between the hard-sphere and Lennard-Jones correlation functions are due to the finite duration time of repulsive force collisions. The attractive forces need not be considered.

Rotational Motion of Molecules in Liquids

In the previous section we introduced two basic ideas. The first is that the motion of molecules in dense fluids is determined mainly by the repulsive parts of the intermolecular potentials. As a result, for liquids composed of spherical particles, the dynamic structure is intimately related to that of a hard-sphere system. The second idea is that the dynamics of hard spheres can be described qualitatively in terms of successive uncorrelated binary collisions.

These concepts have been used recently to develop a theory of rotational motion of molecules in liquids.²⁶ We describe below some of the principal results of that theory.

Within the context of the uncorrelated binary collision approximation, the single particle rotational motion of linear or spherical top molecules is associated with *one* rotational "relaxation time" τ_ω which is defined by²⁶

$$\tau_\omega^{-1} = (N-1) [\langle \mathbf{J} \cdot T_{21} \mathbf{J} \rangle / \langle J^2 \rangle]_{\text{rep}} \quad (11)$$

In this equation, \mathbf{J} denotes the angular momentum of molecule 1; there are a total of N molecules in the system; and T_{21} denotes the zero frequency part of the binary collision operator associated with the repulsive parts of the intermolecular potential. The subscript "rep" indicates that the ensemble average, $\langle \dots \rangle$, is the average appropriate to the repulsive force system; the attractive interactions are neglected. When the molecular shape is fairly spherical, τ_ω^{-1} can be expressed in terms of the Enskog relaxation time²⁶

$$\tau_\omega^{-1}(T, \rho) = \alpha \tau_E^{-1}(T, \rho) \quad (12)$$

Here, we have emphasized the explicit temperature and density dependence. The parameter α is related to the efficiency with which a binary collision can change the angular momentum of a molecule. It appears to be a relatively weak function of temperature.³³

The angular momentum relaxation time, τ_J , is defined as the zero frequency part of the angular momentum autocorrelation function; *i.e.*

$$\tau_J = \int_0^\infty [\langle \mathbf{J} \cdot \mathbf{J}(t) \rangle / \langle J^2 \rangle] dt \quad (13)$$

(33) However, the associated hard-sphere diameter needed to calculate τ_E is a weak but important function of temperature. This temperature dependence must be included when calculating τ_ω from eq 12 because τ_E is a very sensitive function of the hard-sphere diameter. See ref 26.

The binary collision theory derives the approximate result that

$$\tau_J \approx \tau_\omega \quad (14)$$

Equations 14 and 12 provide a simple theory for the density and temperature dependence of τ_J which can be checked by nmr experiments performed on high-density fluids. Preliminary comparison with experiment indicates that the theory is fairly accurate.^{26,34} The physical picture associated with eq 14 is reasonable. From the definition of τ_J , we expect that τ_J should be proportional to the inverse of the average collision frequency since each collision should help a molecule "forget" about its initial angular momentum. It can be shown that the collision frequency is proportional to τ_E^{-1} . Thus, we expect $\tau_J \propto \tau_E$, which is what eq 14 says.

The orientational correlation functions measured by ir experiments²⁸ (eq 15) and by Raman scatter-

$$C_1(t) = \langle \mathbf{u} \cdot \mathbf{u}(t) \rangle = \langle P_1[\mathbf{u} \cdot \mathbf{u}(t)] \rangle \quad (15)$$

ing²⁸ (eq 16) can also be described with the binary

$$C_2(t) = \langle P_2[\mathbf{u} \cdot \mathbf{u}(t)] \rangle \quad (16)$$

collision theory. In these equations, $\mathbf{u}(t)$ denotes the unit vector parallel to an axis of molecule 1 at time t , and $P_l(x)$ is the l th Legendre polynomial of x . The results of the theory are expressed most simply in terms of the Laplace transforms of $C_l(t)$; they are

$$\tilde{C}_l(s) \approx \tilde{C}_l^{(1d)}(s + \tau_\omega^{-1}) / [1 - \tau_\omega^{-1} \tilde{C}_l^{(1d)}(s + \tau_\omega^{-1})] \quad (17)$$

(34) J. DeZwaan, R. J. Finney, and J. Jonas, *J. Chem. Phys.*, **60**, 3223 (1974).

where $\tilde{C}_l^{(1d)}(s)$ denotes the Laplace transform of $C_l(t)$ for a system of ideal gas (free) molecules. Equations 17 and 14 constitute Gordon's J diffusion model approximation for $C_l(t)$.³⁵ Experimental tests indicate that the approximation is qualitatively accurate.^{26,34,36} We note that the *microscopic* theory used to derive eq 17 does not require one to adopt the unphysical assumptions that are often attributed to Gordon's results. The interested reader should see ref 26.

In summary, we have emphasized the following concept: at the high densities which characterize most of the liquid phase, the dynamic and static structures of liquids are dominated by steric (excluded volume) effects. This idea, together with the approximation that the dynamics of hard spheres can be described in terms of uncorrelated binary collisions, gives rise to specific predictions about the density and temperature dependence of several relaxation times and correlation functions. These predictions should be qualitatively accurate for high density liquids composed of fairly spherical molecules. Further, the predictions can be tested by nmr, ir, and Raman experiments. We hope that in the near future constant density and temperature experiments will be performed on dense fluids to investigate fully the strengths and limitations of the theory we have described.

The research reviewed in this article has been supported by grants from the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society. Both are gratefully acknowledged.

(35) R. G. Gordon, *J. Chem. Phys.*, **44**, 1830 (1966).

(36) R. A. Assink and J. Jonas, *J. Chem. Phys.*, **57**, 3329 (1972).

The Role of High-Pressure Kinetics in Studies of the Transition States of Diels-Alder Reactions

James R. McCabe and Charles A. Eckert*

Department of Chemical Engineering, School of Chemical Sciences, University of Illinois, Urbana 61801

Received July 9, 1973

All chemists and chemical engineers dealing in any way with a chemical reaction must eventually investigate the properties of the reaction transition state.

Charles Eckert received his S.B. and S.M. degrees from Massachusetts Institute of Technology. After completion of Ph.D. work at Berkeley under John Prausnitz in 1964, he spent a year as NATO Postdoctoral Fellow at the Laboratoire des Hautes Pressions in France, and then joined the faculty of the University of Illinois, where he is Professor of Chemical Engineering. His major research interests are the applications of molecular thermodynamics to problems in phase equilibria and chemical kinetics and high-pressure solution kinetics.

James McCabe received the Ph.D. degree from the University of Illinois, Urbana, working with Professor Eckert. He is in the Process Engineering Department of Chevron Research Company, Richmond, Calif.

Much can be and has been learned by conventional research on rates, activation energies, and solvent and substituent effects, all at atmospheric pressure. High-pressure kinetic studies, however, offer yet another probe, yielding information unobtainable by other means, yet invaluable in elucidating the structure and properties of the reaction transition state.

High-pressure kinetics in solution permits observation of the volume of activation of a chemical reaction

$$\Delta v^\ddagger = -RT(\partial \ln k / \partial P)_T \quad (1)$$