82. K. N. Mendis, unpublished results.
83. D. C. Kaushal *et al.*, *J. Immunol.* **131**, 2557 (1983).
84. P. G. Harte, N. Rogers, G. A. T. Targett, *Nature (London)* **316**, 258 (1985).
85. J. Rener, P. M. Graves, R. Carter, J. L. Williams, T. R. Burkot, *J. Exp. Med.* **158**, 976 (1983).
86. S. Peiris and K. N. Mendis, unpublished data.
87. A. N. Vermeulen *et al.*, *Mol. Biochem. Parasitol.* **20**, 155 (1986).
88. I. Quakyi, unpublished data.
89. R. Carter, G. Bushell, A. Saul, P. M. Graves, C. Kidson, *Infect. Immun.* **50**, 102 (1985); A. N. Vermeulen *et al.*, *Dev. Biol. Stand.* **62**, 91 (1985).
90. P. M. Graves *et al.*, *Infect. Immun.* **48**, 611 (1985); R. Carter, unpublished results.
91. R. Carter and D. C. Kaushal, *Mol. Biochem. Parasitol.* **13**, 235 (1984); N. Kumar and R. Carter, *ibid.* **14**, 127 (1985); C. A. Grotendorst, N. Kumar, R. Carter, D. C. Kaushal, *Infect. Immun.* **45**, 775 (1984).
92. A. H. Cochrane *et al.*, *Mol. Biochem. Parasitol.* **14**, 111 (1985).
93. S. Sharma, P. Svec, G. H. Mitchell, G. N. Godson, *Science* **229**, 779 (1985).
94. D. Walliker, *Adv. Parasitol.* **22**, 217 (1983).
95. J. S. McBride, D. Walliker, G. Morgan, *Science* **217**, 254 (1982); J. S. McBride, C. I. Newbold, R. Amand, *J. Exp. Med.* **161**, 160 (1985); S. Thaithong *et al.*, *Trans. R. Soc. Trop. Med. Hyg.* **78**, 242 (1984); J. A. Lyon, R. H. Geller, J. D. Haynes, J. D. Chulay, J. L. Weber, *Proc. Natl. Acad. Sci. U.S.A.* **83**, 2989 (1986).
96. A. A. Holder *et al.*, *Nature (London)* **317**, 270 (1985); M. Mackay *et al.*, *EMBO J.* **4**, 3823 (1985); J. L. Weber, W. M. Leininger, J. A. Lyon, *Nucleic Acids Res.* **14**, 3311 (1986).
97. R. J. Howard, J. W. Barnwell, V. Kao, *Proc. Natl. Acad. Sci. U.S.A.* **80**, 4129 (1983).
98. J. W. Barnwell, R. J. Howard, H. A. Coon, L. H. Miller, *Infect. Immun.* **40**, 985 (1983).
99. M. Hommel, P. H. David, L. D. Oligino, *J. Exp. Med.* **157**, 1137 (1983).
100. L. H. Miller *et al.*, *J. Immunol.* **132**, 438 (1984).
101. P. H. David, D. E. Hudson, T. J. Hadley, F. W. Klotz, L. H. Miller, *ibid.* **134**, 4146 (1985); F. W. Kotz, D. Hudson, L. H. Miller, *J. Exp. Med.*, in press.
102. A. H. Cochrane, R. W. Gwadz, J. W. Barnwell, K. K. Kawboj, R. S. Nussenzweig, *Am. J. Trop. Med. Hyg.* **35**, 479 (1986); V. Enea, M. R. Galinski, E. Schmidt, R. W. Gwadz, R. S. Nussenzweig, *J. Mol. Biol.* **188**, 721 (1986).
103. A. Kilejian, *J. Biol. Chem.* **249**, 4650 (1974).
104. J. V. Ravetch, R. Feder, A. Pavlovec, G. Blobel, *Nature (London)* **312**, 616 (1984).
105. J. V. Ravetch, J. Kochan, M. Perkins, *Science* **227**, 1593 (1985).
106. R. J. M. Wilson, I. A. McGregor, P. Hall, K. Williams, R. Bartholomew, *Lancet* **1969-II**, 201 (1969).
107. A. F. Cowman *et al.*, *Cell* **40**, 775 (1985).
108. A. Saul, J. Cooper, L. Ingram, R. F. Anders, G. V. Brown, *Parasit. Immunol.* 7, 587 (1985).
109. R.S.N. and V.N.'s experimental work has been financially supported by the Agency for International Development (DPE 0453-A-00 5012 00), the MacArthur Foundation, the National Institutes of Health (P01-AI17429), the Rockefeller Foundation and the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases. R.C. and L.H.M.'s work has been supported in part by the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases and the Rockefeller Foundation. M.F.G. is a recipient of a Neil Hamilton Fairley Fellowship from N.H. and M.R.C. (Australia) and of a Fulbright Postdoctoral Award.

Randomly Exact Methods

J. D. Doll and D. L. Freeman

Important advances in the understanding of "random" processes have produced a variety of stochastic algorithms that offer unprecedented scope and utility in the study of physical systems. These algorithms represent a departure from the usual philosophy inherent in the study of many-body problems and have a number of significant features. Chief among these features are simplicity, weak dependence on dimensionality, and ease of transition between classical and quantum-mechanical descriptions. These methods are also readily adapted for use on massively parallel computer architectures. These new stochastic methods represent a valuable addition to the tools available for the analysis of both equilibrium and time-dependent many-body problems.

A curious feature of physical science is that there are few problems for which the fundamental equations of the underlying theory can be solved exactly and the resulting predictions compared directly with macroscopic observations. The cases for which this can be done are vital for testing the adequacy of basic theories, but mathematical difficulties prevent us from making such connections on a general basis. Our understanding of macroscopic physical phenomena, therefore, is of necessity based on intuition formed from these few important examples and from results of approximate calculations. Often these approximate calculations are inadequate and typically contain untested assumptions. In areas such as chemistry and condensed matter physics, this situation is especially frustrating since it is generally felt that the underlying microscopic theory is complete. Were we in a position to solve the basic equations exactly, meaningful predictions of the equilibrium and time-dependent properties of materials, both real and hypothetical, would be possible. Such predictions could be of significant assistance, for example, in the search for new substances with desirable physical, chemical, or biological properties. A new class of numerical methods based on the study of random processes (*1, 2*) offers the possibility of a general solution to this unsatisfactory situation. These "randomly exact" methods represent an unusual combination of simplicity, generality, and power.

Physical science and mathematics are largely concerned with the study of order. Thus the study of random processes is, at first glance, somewhat odd. Experience has shown, however, that many apparently random processes when more deeply studied exhibit regular behavior. This being the case, a common viewpoint concerning random phenomena could be termed "hostile tolerance," hostile because of the implicit and often untidy chaos, but tolerant since much of the chaos can ultimately be understood or eliminated. In this article we describe the evolution of this position of tolerance into one of advocacy.

The study of random phenomena has historically yielded a rich harvest of interesting mathematics. An important example is the distribution of random errors. Repeated measurements of a well-

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defined property made with the use of an instrument having finite resolution will result in a collection of values distributed about a unique limiting mean. That the results contain statistical scatter is not surprising. That the distribution of the measurements about the mean tends to be of a particularly simple and universal form, the Gaussian distribution, is, however, an intriguing expression of order.

A second, and perhaps ultimately the richest, example of order in a random process is found in Brownian motion (*1, 3*). Originally observed by the botanist Robert Brown in the early 19th century as the erratic movements of small particles suspended in liquids, this phenomenon provided a crucial link in the development of atomic theory. Viewed in modern molecular terms, the collisions of solvent molecules with the suspended particles cause these particles to execute a random walk. What thus appears as macroscopic random motion of the suspended particles is, upon closer analysis, only a reflection of the ordinary, atomic scale motion of the solvent. Viewed on this microscopic scale, Brownian motion contains, adapting Kac's words (*4*, p. 70), "no coins, no chance, no mystery." A deeper study of Brownian motion has led to a number of other important discoveries. Wiener's formulation of Brownian motion in terms of path integrals (*5*) and his harmonic analysis of random processes (*6*) are two important examples. Much of the motivation for the theory of fractals (*7*) drew heavily on ideas and images from Brownian motion theory. Such studies have also refined our understanding of the connection between reversible and irreversible processes.

Having found order in chaos, one might have expected that we would have been satisfied. In the past 40 years, however, we have witnessed the emergence of another direction of investigation in random processes, a line of development that amounts essentially to an inversion of the philosophy sketched above (*4, 8*). Rather than being the objects of study, random processes are now frequently the tools by which "regular" systems are investigated. No longer viewed as unsettling, these processes are now routinely added to problems that contain no physically random aspects. The driving force behind this about-face is twofold. On the conceptual level, one often finds that addition of suitable noise can actually simplify rather than complicate a problem. On the practical level, the development of large computing machines makes it possible to utilize these stochastic approaches quite efficiently. In fact, random methods now form the basis of practical, nonapproximate tools for the study of many-body problems.

Monte Carlo Integration Methods

Classical equilibrium statistical mechanics (*9*) is an example of a field in which stochastic algorithms have made important contributions. Basic to this field is the calculation of thermodynamic properties starting from microscopic force laws. These properties are generally expressed as averages over well-defined, but often complicated probability distribution functions. The averages are of the generic form,

$$\langle f \rangle = \int dx\, \rho(x)\, f(x) / \int dx\, \rho(x) \qquad (1)$$

where x represents a set of coordinates, $f(x)$ is the quantity to be averaged expressed as a function of those coordinates, and $\rho(x)$ describes the equilibrium distribution of possible coordinate values for the system under study. Except for a few special cases, these averages are not calculable by analytic means. Furthermore, ordinary numerical methods, such as Gauss quadrature schemes, are not especially useful since the integrations are typically of quite high dimension.

In the early 1950's Metropolis *et al.* (*10*) devised an ingenious stochastic method for the evaluation of averages of the type shown in Eq. 1. Their approach was a special case of what have become known as Monte Carlo methods. In these methods, as can be guessed from the colorful name, one devises a suitable random "game" in which the answer to the question under study emerges as the game is played. For the integration problem above, the game is a random walk in x-space designed in such a way that the probability of visiting a particular point x is proportional to the statistical weight for that point, $\rho(x)$. So constructed, the set of points visited in an N-step random walk, (x_n), $n = 1, \ldots, N$, can be used to estimate $\langle f \rangle$ in Eq. 1 according to the expression

$$\langle f \rangle = \sum_{n=1}^{N} f(x_n)/N \qquad (2)$$

For finite N this estimate will have a statistical uncertainty associated with incomplete sampling that can be shown to be proportional to $\sigma_f/\sqrt{N}$, where σ_f is the standard deviation of f, and is defined by

$$\sigma_f = (\langle f^2 \rangle - \langle f \rangle^2)^{1/2} \qquad (3)$$

The Metropolis method has a number of remarkable features. At its core the method is a curious one since it represents the exchange of a well-defined problem, that of computing integrals, for one involving the study of an artificially constructed random process. This exchange, however, produces an algorithm with significant advantages. Chief among these advantages is that the resulting method applies with equal ease to small or large dimensional problems, producing the $1/\sqrt{N}$ convergence rate in either case. The method has the additional feature of variable resolution: short random walks rapidly produce order-of-magnitude estimates whereas more extensive random walks permit further refinement. This variable resolution allows the precision of a calculation to be adjusted to match the particular problem under study.

Of particular importance is the simplicity of the Metropolis method and its convenience with respect to use on present and future computing machines. Anticipating parallel computing applications, it is important to note that Monte Carlo games can be played independently, implying that these methods can easily take advantage of relatively simple and large-scale parallel machines.

The Metropolis approach is extensively (*11*) used, with one class of applications, "numerical experiments," being especially valuable. The calibration of approximate analytic theories is an important task. If well understood with respect to accuracy and limitations, predictions of such theories can be used with confidence. Without such calibrations, such methods frequently are reduced to expressions of hope. Comparisons of the predictions of approximate methods with experimental results are generally ambiguous since the effective force laws describing the interaction of composite systems (such as atoms or molecules) are themselves often unknown. Since the Metropolis method can proceed, without untestable assumptions, from the specification of a microscopic force law to a prediction of equilibrium properties, it can serve as a source of synthetic data on model systems with specified interactions against which the quality of approximate analytic theories can be judged unambiguously. Conversely, one can probe the quality of a particular interaction force law (empirical or otherwise) by comparing the results of numerically exact Monte Carlo predictions with laboratory data.

The development of recent theories of dense fluids illustrates the role of Monte Carlo methods as numerical experiments (*12*). Such experiments make it possible, for example, to discern those portions of the microscopic interactions that are principally responsible for determining fluid structure. Since nature has the final word concerning its microscopic forces, it would be difficult to devise a physical

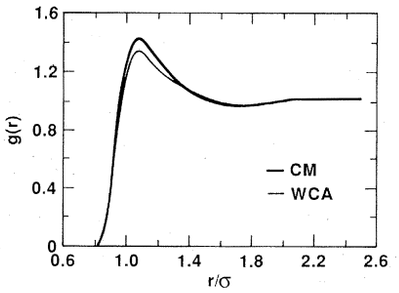

Fig. 1. Radial distribution functions, $g(r)$, for a simple Lennard-Jones fluid computed via classical Monte Carlo methods. Results obtained by using the full interaction are denoted by CM and those obtained by using the repulsive portion of the interaction (*12*) are denoted by WCA. The temperature is $kT/\epsilon = 5.0$ and the density is $\rho\sigma^3 = 0.365$.

experiment that would directly probe the assumption, for example, of short-range, packing dominance of dense fluid structure. Designing such an unambiguous test using Monte Carlo methods, however, is a relatively simple matter. Figure 1 shows the results of a Monte Carlo calculation of a particular thermodynamic property, the radial distribution function, for a chosen thermodynamic state of a simple classical fluid. The radial distribution function denotes the ratio of the density observed in the fluid as a function of the distance from a specified atom compared with the overall bulk fluid density. In one set of classical mechanics calculations (CM), the atoms in the fluid are assumed to interact by means of pairwise additive Lennard-Jones potentials,

$$V_{LJ}(r/\sigma) = 4\epsilon[(\sigma/r)^{12} - (\sigma/r)^6]$$

where ϵ and σ are energy and distance parameters, respectively. In the second set of results (WCA), the pair interaction is taken to be the repulsive portion of the Lennard-Jones interaction

$$V_{WCA}(r/\sigma) = 4\epsilon[(\sigma/r)^{12} - (\sigma/r)^6] + \epsilon, \text{ for } r < \sigma$$
$$= 0, \text{ otherwise}$$

the Weeks-Chandler-Andersen (WCA) form (*12*). The agreement of the two results in Fig. 1 is a measure of the quality of the assumption of the dominance of short-ranged, repulsive forces for this example. Similar numerical experiments provided the motivation for the development of simple perturbation theories of dense fluids organized around short-range reference systems (*12*). The development of these theories is an example of the intelligent, interactive combination of analytic theory and numerical experiment.

Stochastic Dynamics

In the preceding section we have examined the application of random methods to a broad class of equilibrium problems. Variations of the same algorithms are also well suited to investigation of time-dependent problems and represent an important generalization of familiar molecular dynamics methods (*13*). Using these generalizations, we can study stochastic differential equations with only minor modifications of the techniques that have been devised for the study of their ordinary counterparts.

As a particular example of how these dynamical applications proceed, consider the Langevin equation for a free particle,

$$dp/dt = -\gamma p + R(t) \quad (4)$$

This equation describes the time development of the momentum, p, of a particle in a viscous medium, a medium that supplies both a frictional force, characterized by the constant γ, and random thermal noise, denoted by $R(t)$. Since we are ultimately interested in stochastic differential equations that do not have simple analytic solutions, we seek a general approach to the treatment of Eq. 4. The required approach is implicit in Chandrasekhar's classic review (*3*) of Brownian motion. If we discretize Eq. 4 on a time grid where $t_n = n\Delta t$, it is not difficult to show that if Δt is small, then Eq. 4 implies that

$$p(t_{n+1}) = p(t_n) - \gamma p(t_n)\Delta t + B_n \quad (5)$$

Here the Δt term arises from the systematic frictional force while B_n is defined in terms of the random force by

$$B_n = \int_{t_n}^{t_{n+1}} R(s)\, ds \quad (6)$$

From the properties of Brownian noise, it can be shown that B_n is a Gaussian random variable with a mean and second moment specified by

$$\langle B_n \rangle = 0 \quad (7a)$$
$$\langle B_n B_l \rangle = \delta_{nl}(2m\gamma kT\Delta t) \quad (7b)$$

where m is the particle mass, k is Boltzmann's constant, and T is the temperature of the medium. Equations 5 through 7 provide a recipe by which we can solve the original Langevin equation numerically in the same fashion as we would an ordinary differential equation, except that we must add suitably constructed "noise" to our procedure. This noise is not arbitrary, but, as indicated in Eq. 7b, must be balanced with the frictional dissipation to ensure thermal equilibrium. The present method avoids the pitfall of attempting to develop quadrature expressions for the time integral of the random force, a difficult task in view of its variation on all possible time scales. It is straightforward to generalize the above approach to the case of many-body interacting systems and to problems with time-dependent frictional terms requiring solution of the generalized Langevin equation (*14*).

Numerical Langevin equation methods, such as those sketched above, have played a valuable role in the study of condensed phase systems. A variety of such approaches have been used to study gas-molecule/solid-surface collision processes, for example (*14, 15*). For this problem, it is unnecessary and inefficient to describe in detail the time evolution of the entire lattice since in a typical gas-solid collision the incident species interacts strongly and directly with only a relatively small number of lattice atoms. The remainder of the lattice functions as a heat bath capable of exchanging energy with the interaction region. This physical observation translates mathematically into the replacement of the equations of motion for the entire adsorbate-lattice system with Langevin-like equations for a reduced set of "primary" variables. By means of this rigorous transformation, the gas-solid study, originally involving the study of a large set of ordinary differential equations, is reduced to the study of a relatively small set of stochastic equations. The use of random processes is a general device to reduce the dimensionality of the problem under study. Extensions of these methods to study the structure and dynamics of molecular fluids have been developed by Adelman (*16*). Details of numerical Langevin applications are discussed extensively elsewhere (*14, 15*).

Related stochastic dynamics methods are linked to the original Metropolis equilibrium method and can be used to justify the frequent use of that approach as a pseudo-dynamical technique. To see this connection more explicitly, consider a particularly simple case in which the classical equations of motion are propagated numerically, constrained so that the velocities are completely thermalized prior to each iteration. Although no longer Newtonian, the coordinates generated by such a trajectory will be described by a Boltzmann distribution. Since particles are moved according to a procedure that takes into account their interactions, one might expect that this sampling procedure would be efficient. If the propagation of the classical equations of motion is inaccurate

because of numerical round-off error or inadequate numerical integration methods, then one must take additional steps to assure that a proper thermal distribution is produced. This means that rather than accepting the results of the stochastic algorithm directly, they must first be "filtered," with a secondary random process chosen to produce the desired statistical distribution. Operationally, this means that the stochastic algorithm is used to generate "trial" configurations that are subsequently accepted or rejected according to the principles of detailed balance. The Metropolis Monte Carlo method corresponds to a particular choice of the stochastic algorithm used to generate trial configurations, a choice that incorporates thermal randomization, but one that ignores the microscopic forces in the subsequent propagation (*17*). The microscopic forces enter the basic Metropolis procedure only through the secondary rejection process.

Monte Carlo Path-Integral Methods

The discussion has thus far been principally concerned with the equilibrium and time-dependent applications of stochastic methods to classical-mechanical problems. These methods, however, have broader applicability: Brownian motion theory and quantum mechanics can be coupled for the study of analogous problems. This flexibility and ease of transition between quantum and classical descriptions is a particularly valuable characteristic of the current approaches. Moreover, the ability to generate effectively exact solutions to the basic quantum-mechanical equations for complex, interacting, many-body problems offers us an unprecedented analytic tool.

The origins and use of quantum Monte Carlo methods to study ground-state solutions to the Schrodinger equation have been reviewed by Ceperley and Alder (*18*). In this approach, the isomorphism between the wave equation in complex time and the diffusion equation with branching is exploited to develop a Monte Carlo diffusion algorithm that generates the solution to the original quantum-mechanical problem. Applications of this approach show great promise for both few- and many-body problems.

Monte Carlo methods are also available to treat equilibrium and dynamics problems at finite temperature. Here the general approach is to concentrate attention on the quantum-mechanical density matrix, $\rho(x',x,\beta)$, defined in terms of the Hamiltonian H, as

$$\rho(x',x,\beta) = \langle x'|\exp(-\beta H)|x\rangle \quad (8)$$

where $\beta = 1/kT$. Knowledge of ρ for real values of β is sufficient to calculate equilibrium properties. If, in addition, we have knowledge of ρ for complex β, then we can also extract dynamical information.

Various practical procedures for constructing the relevant density matrix elements can be developed, starting with a path-integral representation (*18–20*). In this approach we parameterize the paths that enter into the formal representation of the density matrix, thereby transforming the path-integral problem into a high-dimensional, but otherwise ordinary problem in integration. The operational result of this procedure is to transform the original quantum-mechanical problem in the variable x into an effective classical problem in an enlarged space that contains the original coordinate plus all path variables. Chandler and Wolynes have discussed this "classical isomorphism" extensively (*19*). The point for the present discussion is that ordinary Monte Carlo integration methods, familiar within classical-mechanical applications, can thus be brought to bear on quantum-mechanical problems. This development gives us the same type of general, exact stochastic methods for quantum-mechanical problems that have previously proved so useful within classical mechanics.

Table 1. Calculated Gibbs free energy of formation of a 13-particle cluster of argon atoms as a function of temperature (T) at a pressure of 1 atm. Quoted are results of both classical (CM) and quantum-mechanical (QM) Monte Carlo calculations. Approximate quantum-mechanical results (*24*) are shown for comparison (HPW). Numbers in parentheses are Monte Carlo uncertainties in the last reported digit.

T (K)	$\Delta G_{CM}/kT$	$\Delta G_{QM}/kT$	$\Delta G_{HPW}/kT$*
10	−408.2 (3)	−383.6 (4)	−383.8
15	−244.4 (6)	−232.0 (6)	−220.3
20	−161.6 (5)	−158.2 (5)	−137.6
25	−117.4 (4)	−115.7 (4)	− 87.7
30	− 88.1 (5)	− 86.9 (5)	− 54.4

*From (*24*).

The scope of applications of path-integral Monte Carlo methods is expanding rapidly (*21*). We consider here a few such examples, each chosen both to illustrate a generic application and to indicate the general insight that such methods can supply.

The study of molecular clusters is important both from a conceptual and from a practical point of view. Studies of cluster properties as a function of their size make it possible, for example, to probe the onset of bulklike behavior. Cluster studies enable us to examine the process of solvation and the effects of solvent cages on the dynamics of various molecular processes. Knowledge of the thermodynamic properties of nucleation microclusters would, in particular, enable us to estimate the kinetics of homogeneous nucleation and would lead to an improved understanding of condensation phenomena (*22, 23*). Methods aimed at predicting the thermodynamic properties of clusters have to contend with problems that are simultaneously many-body, anharmonic, and quantum-mechanical in nature. Typical approaches to such problems have tended to concentrate on one or another of these aspects, proceeding on the assumption that the others represented small effects. Using path-integral Monte Carlo methods, it is possible to study the properties of molecular clusters without resorting to such approximations. Table 1 lists some representative results of a particular path-integral Monte Carlo study of the equilibrium properties of prototype clusters. Shown are the changes in the Gibbs free energies resulting from the formation of 13-particle argon clusters from dispersed atoms. To investigate quantum-mechanical and anharmonic effects, we computed results (*20*) by using a variety of methods, including classical Monte Carlo (CM), path-integral Monte Carlo (QM), and an approximate quantum-mechanical calculation (*24*) based on harmonic force law assumptions (HPW). For simplicity the argon atoms in the Monte Carlo calculations were assumed to interact by pairwise Lennard-

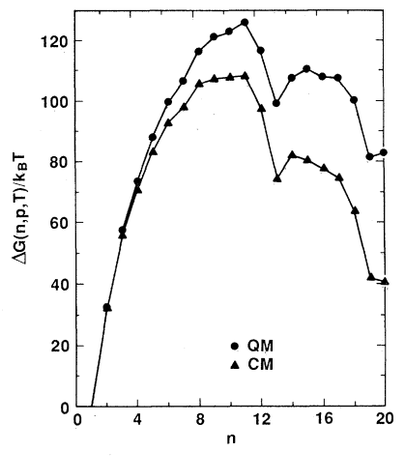

Fig. 2. Gibbs free energies of formation of n particle argon clusters at a temperature of 10 K and a pressure of 3.34×10^{-18} atm. Both quantum (QM) and classical (CM) Monte Carlo results are indicated (*20*).

Jones potentials. Table 1 illustrates that at low temperatures the clusters are quantum-mechanical in nature, but that at these low temperatures their behavior is essentially harmonic in character. Conversely, at high temperatures the clusters are appreciably anharmonic but classical. Most importantly, there is a temperature range over which the argon clusters are neither classical nor harmonic in their behavior, implying that attempted treatments of cluster properties based on either of these assumptions will, in general, fail over some finite temperature range (Table 1). Figure 2 illustrates the quantum and classical free energies of formation of these argon clusters as a function of cluster size for a particular temperature and pressure. The two sets of results differ with respect to details, implying that for these particular conditions quantum effects are significant. Both sets of results predict a prominent free-energy barrier, commonly discussed in terms of surface effects, and both predict "magic number" behavior, local free energy minima associated with cluster sizes that are thermodynamically metastable with respect to growth or decay.

These cluster results emphasize a common pitfall in the analysis of experimental data. Empirical microscopic interactions are often inferred by fitting approximate theories to experimental data. If the predictions of the approximate theories are inaccurate, then the interactions extracted by such a procedure will necessarily be flawed. Exact methods of the type discussed above avoid this difficulty.

Quantum-mechanical corrections to extended systems have also been studied with the use of Monte Carlo path-integral methods. Figure 3 illustrates one such prototypical application. Shown are the classical and quantum-mechanical radial distribution functions computed for a particular model of a specific thermodynamic state of liquid helium. Quantum corrections are large for this system. Extensive applications of path-integral methods to condensed phase systems, including those with appreciable exchange effects, are discussed elsewhere (*25–27*).

One exciting recent development is the use of Monte Carlo path-integral methods in quantum dynamics. As emphasized by a number of investigators (*28–32*), knowledge of the density matrix for complex temperature is sufficient to extract a variety of dynamical information. Current approaches are limited to relatively short-time information, but even this information is adequate for a variety of important problems. The origin of this short-time limitation is related to the mathematical problems inherent in performing Monte Carlo integrations of rapidly oscillatory integrands, a situation that arises as a result of the complex exponential in the propagator. Significant progress in this area is likely.

Conclusions

The study of random processes has proved to be a fruitful endeavor. Historically, such studies have provided the foundations of atomic theory and have played a continuing role as an important bridge between mathematics and physical science. Random processes, having spawned much of current microscopic physical theory, are increasingly becoming the tools for its analysis. Stochastic approaches now form the basis of general methods for the analysis of equilibrium and time-dependent problems in both classical and quantum physics. These approaches are subtle in construction, simple in practice, and increasingly important in physical science.

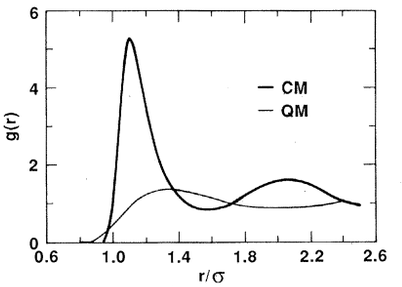

Fig. 3. Radial distribution functions, $g(r)$, for liquid helium computed by both quantum (QM) and classical (CM) Monte Carlo methods. The temperature is $kT/\epsilon = 0.5$ and density is $\rho\sigma^3 = 0.365$ (*26*).

REFERENCES AND NOTES

1. For a collection of several classic works on the study of random processes, see *Selected Papers on Noise and Stochastic Processes*, N. Wax, Ed. (Dover, New York, 1954).
2. For a critical discussion of the nature of randomness, see G. Kolata, *Science* **231**, 1068 (1986).
3. S. Chandrasekhar, *Rev. Mod. Phys.* **15**, 1 (1943).
4. M. Kac, *Enigmas of Chance* (Harper and Row, New York, 1985).
5. See *Norbert Wiener: Collected Works*, vol. 1, P. Masani, Ed. (MIT Press, Cambridge, 1976), for several references.
6. See *Norbert Wiener: Collected Works*, vol. 2, P. Masani, Ed. (MIT Press, Cambridge, 1979).
7. B. B. Mandelbroit, *Fractals: Form, Chance, and Dimension* (Freeman, San Francisco, 1977); *Fractical Geometry of Nature* (Freeman, San Francisco, 1982).
8. S. M. Ulam, *Adventures of a Mathematician* (Scribners, New York, 1976).
9. D. A. McQuarrie, *Statistical Mechanics* (Harper and Row, New York, 1976).
10. N. Metropolis, A. W. Rosenbluth, M. N. Rosenbluth, A. H. Teller, E. Teller, *J. Chem. Phys.* **21**, 1087 (1953).
11. J. P. Valleau and S. G. Whittington, in *Modern Theoretical Chemistry*, B. J. Berne, Ed. (Plenum, New York, 1977), vol. 5, pp. 137–168.
12. D. Chandler, *Annu. Rev. Phys. Chem.* **29**, 441 (1978); ———, J. D. Weeks, H. C. Andersen, *Science* **220**, 787 (1983); J. A. Barker and D. Henderson, *J. Chem. Phys.* **47**, 4714 (1967); *Rev. Mod. Phys.* **48**, 587 (1976); (*9*), chap. 14.
13. For a recent review see J. Kushick and B. J. Berne, in *Modern Theoretical Chemistry*, B. J. Berne, Ed. (Plenum, New York, 1977), vol. 6, pp. 41–63.
14. S. A. Adelman and J. D. Doll, *Acc. Chem. Res.* **10**, 378 (1977).
15. J. C. Tully, *Annu. Rev. Phys. Chem.* **31**, 319 (1980).
16. S. A. Adelman, *Adv. Chem. Phys.* **44**, 1432 (1980).
17. P. J. Rossky, J. D. Doll, H. L. Friedman, *J. Chem. Phys.* **69**, 4628 (1978).
18. D. Ceperley and B. Alder, *Science* **231**, 555 (1986).
19. D. Chandler and P. Wolynes, *J. Chem. Phys.* **74**, 4078 (1980).
20. D. Freeman and J. Doll, *ibid.* **82**, 462 (1985) and references therein.
21. See, for example, the proceedings of the Metropolis 70th birthday quantum Monte-Carlo meeting [published as *J. Stat. Phys.* **43** (Nos. 5/6) (1986)] for additional references.
22. F. F. Abraham, *Homogeneous Nucleation Theory* (Academic Press, New York, 1974).
23. J. J. Burton, in *Modern Theoretical Chemistry*, B. J. Berne, Ed. (Plenum, New York, 1977), vol. 5, pp. 195–234.
24. M. R. Hoare, P. Pal, P. P. Wegener, *J. Colloid Interface Sci.* **75**, 126 (1980).
25. E. L. Pollack and D. Ceperley, *Phys. Rev. B* **30**, 2555 (1984).
26. J. D. Doll, D. L. Freeman, R. D. Coalson, in preparation.
27. D. Ceperley and E. L. Pollack, *Phys. Rev. Lett.* **56**, 351 (1986).
28. E. C. Behrman, G. A. Jongeward, P. G. Wolynes, *J. Chem. Phys.* **79**, 6277 (1983).
29. W. H. Miller, S. D. Schwartz, J. W. Tromp, *ibid.*, p. 4889.
30. D. Thirumalai and B. J. Berne, *ibid.*, p. 5029.
31. J. D. Doll, *ibid.* **81**, 3536 (1984).
32. R. D. Coalson, *ibid.* **83**, 688 (1985).

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