

the classical equations of motion. The results of the previous section show that computed rates for the A + A → products case should not be compared to the classical integrated rate law (6), but rather to the one derived below.

Considering a small, fixed number of molecules is equivalent to setting $\delta n_i = 0$ in (31) or (32), or simply $s = 1$ in (35). In either case the rate law is

$$-\frac{1}{v} \frac{dn}{dt} = (2k_{III}/v^2)n(n-1) \quad (37)$$

where we remove the average notation from n to emphasize that it is fixed and use v rather than V as a reminder that small volumes are required in order for reaction to be observed with a small number of molecules. Equation 37 is readily integrated by the separation-of-variables method to

$$\ln \left(\frac{n}{n-1} \right) = \ln \left(\frac{n}{n-1} \right)_0 + (2k_{III}/v)t \quad (38)$$

in place of (6). For large n , the logarithms in (38) can be expanded to give $1/n$ and $1/n_0$, such that (38) becomes (6) upon multiplication by v . Numerically, the difference between $-\ln(1-1/n)$ and $1/n$ is 5% for $n = 10$ and 1% for $n = 50$. Whether these differences are important depends upon the nature of the computer simulation.

Discussion

The results obtained from the arguments presented above do not change any of the working equations of chemical kinetics; nor have we been able to conceive of any experiments that could test the theoretical results.

The gain for the theory of chemical kinetics is therefore entirely conceptual. Explicit but approximate consideration of the magnitudes of diffusion and reaction rates showed that chemical reaction can proceed either faster or more slowly than dissipation of local concentration fluctuations for conditions typical of chemical kinetics experiments. Accordingly, an investigation of whether these fluctuations may affect the interpretation of macroscopic rate measurements in terms of microscopic models was required. Reassuringly, this investigation led to the conclusion that the conventional rate laws and integrated rate laws for the three cases tested proved to be

completely correct, although for case III the conventional derivation itself was found to be incorrect.

It is certain that other cases exist in which the effects of fluctuations must prove *not* to average out to the conventional results. There are many possible elaborations of the ones we tested which could be considered to this end. One would of course again have to consider whether experimental conditions exist where the magnitude and dissipation rates of the fluctuations permit these effects to occur in the real world. It is possible that computer experiments might prove to be an easier route to testing such possible conclusions than laboratory experiments, but there are complex but important reaction mechanisms where fluctuations are already known to play decisive roles in chemical kinetics. These include initiation of polymerization, population genetics, and explosion; extensive experimental and theoretical work has been done on them. Amplification of fluctuations by chemical reaction clearly does not occur, however, for the schematic elementary reactions considered here. It is possible that extensions of the method of investigation used in the present work may permit identification of criteria for instability toward fluctuations that would be useful in a wide range of contexts. Stability tests for more complicated systems are at present most effectively carried out by qualitative analysis of equivalent dynamical systems.¹³

Finally, the geometric difficulties in computing the rate of dissipation of concentration fluctuations suggest that this apparently overlooked topic of fluctuation dynamics may well be of sufficient interest to be worth investigating in depth.

Acknowledgment. Consideration of this problem was suggested to us by the results of computer simulations, done by Dr. Bernhard Nickel in this institute, suggesting a possible difference in the reaction dynamics of distinguishable and indistinguishable particles. The work was carried out while the authors held Senior U.S. Scientist Awards from the Alexander von Humboldt-Stiftung. We thank M. Eigen for the generous hospitality extended to us during this tenure.

(13) M. Eigen and P. Schuster, *Naturwissenschaften*, 65, 7 (1978).

Theory of Brownian Motion in Three Dimensions. Application to Dissipation of Concentration Fluctuations

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The Brownian motion equation is solved for the cases of diffusive motion out of a rectangular parallelepiped and a sphere, assuming equal diffusion coefficients inside and outside the boundary surfaces. Averaging over a uniform initial internal distribution provides probability functions which are required to describe the dissipation of local concentration fluctuations.

Introduction

Local concentration fluctuations in a macroscopically homogeneous solution are readily discussed in equilibrium statistical mechanics, most conveniently in the grand en-

semble formalism, and found to be described as to magnitude by

$$\langle (\delta n)^2 \rangle_{\text{ens}} = \langle n \rangle_{\text{ens}} \quad (1)$$

where $\langle n \rangle_{\text{ens}}$ is the ensemble average number of molecules in a system and δn_i is the difference between n_i , the (in-

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stantaneous) number of molecules in system i , and $\langle n \rangle_{\text{ens.}}^1$. From a dynamic point of view, the value of δn_i in a particular (small) subvolume i of a macroscopically homogeneous solution fluctuates about zero in a random manner and at a rate that depends upon the size and shape of the subvolume and upon the diffusion coefficient of the molecules.

One would think that the dissipation rate of these fluctuations would have been thoroughly investigated, as have dissipations of other fluctuating quantities.² This appears not to be the case, however, probably because this rate is dependent upon the shape of the system (the volume element) considered and because there seems to be little experimental impetus to deal with the theory in exact form. Early in this century there was such an impetus, in connection with quantitative microscopic observations of Brownian motion in colloidal solutions. A theory of concentration fluctuations applicable to the experimental geometries which were used for collecting the fluctuation data was indeed developed by Smoluchowski, who also applied it to discuss the experimental data.³ Aside from his work we have not been able to find any further exact investigations of concentration fluctuations, nor solutions to the corresponding diffusion problems, in the literature. This may be due in part to the practice, attributed to, but as far as we can tell not explicitly introduced by, Onsager,^{4,5} of linearizing the equations of transport which underlie the approach of fluctuating variables to their equilibrium values. To prevent misunderstanding of the object of the present development, we avoid the terms "relaxation", with its connotation of exponential decay, and the equivalent "regression" used by Onsager, in favor of "dissipation" of concentration fluctuations. The applicability of exponential decay functions is discussed later.

In connection with a study of the effects of local concentration fluctuations upon chemical reaction rates⁶ it became necessary to consider the dissipation rates of concentration fluctuations in three-dimensional geometry, which, since it is not particularly appropriate for use with microscopes, was not done by Smoluchowski. The corresponding diffusion problems for spherical and Cartesian geometry are cumbersome to solve and not fully developed in the standard treatises.^{7,8} Since there may be applications for the intermediate and final results in other areas of physical chemistry, we present the analysis and final equations here in some detail.

Smoluchowski's Formulation of Concentration Fluctuation Dissipation

The basic question addressed by Smoluchowski was the following. Suppose that one observes a small volume v out of a large volume V containing N solute molecules, such that the average number of solute molecules present in v , when the observation is continued for a long time, is $\langle n \rangle = N(v/V)$. At a given instant the difference between the

actual number n present in v and the average number is $\delta n = n - \langle n \rangle$. How does δn evolve, on the average, in time? This question requires two assumptions for its resolution: one about the initial distribution of the n molecules in v and the $N - n$ molecules in $V - v$, and one about the correlations of the motions of the molecules. Smoluchowski assumed that the distribution of molecules is everywhere random, or equivalently that the probability distribution is uniform, and that the motions of all molecules are independent. These assumptions reduce the problem to a combinatorics one, which he solved to get a set of complicated probability functions for the evolution of δn . He then showed that these functions can be reduced, by very involved but exact operations, to remarkably simple formulas for the average concentration changes. These are

$$\langle \delta n \rangle = (\langle n \rangle - n_0) \langle P(V - v, t | v, t_0) \rangle \quad (2)$$

$$\langle (\delta n)^2 \rangle = 2 \langle n \rangle \langle P(V - v, t | v, t_0) \rangle \quad (3)$$

where $\langle P(V - v, t | v, t_0) \rangle$ is the average probability that an individual solute molecule, of the n_0 which are located somewhere within v at time t_0 , will be located outside this volume at a later time t .

Equation 2 confirms one's anticipation that while this is intrinsically a first-order process, i.e., that $\langle \delta n \rangle$ is proportional to the fluctuation $(n - \langle n \rangle)$ with a negative proportionality "constant", the fact that $\langle P(V - v, t | v, t_0) \rangle$ is a function of time—rather than a rate constant as would pertain to a true first-order chemical reaction—generates a more complicated function of time than simple exponential decay. Evaluation of the average "escaped" probability $\langle P(V - v, t | v, t_0) \rangle$ enables (2) to become an explicit dissipation equation. Smoluchowski did this for two cases corresponding to the microscope observations: an infinite slab, where diffusion only in the perpendicular coordinate changes n , and a cylinder with reflecting end walls, where only radial diffusion changes n . For the first case he obtained, setting $t_0 = 0$

$$\langle P(V - v, t | v, 0) \rangle = \text{erfc}(\beta) + [1 - e^{-\beta^2}] / \beta \pi^{1/2} \quad (4)$$

where $\beta^2 = h^2/4Dt$, h is the slab thickness, and D the diffusion coefficient, and for the second case

$$\langle P(V - v, t | v, 0) \rangle = e^{-2\beta^2} [I_0(2\beta^2) + I_1(2\beta^2)] \quad (5)$$

where I_0 and I_1 are Bessel functions of imaginary argument and h becomes the cylinder radius. We now evaluate the average escaped probability in three dimensions.

Solution in Cartesian Geometry

Our starting point is the fundamental Brownian motion equation

$$P_x(x, t_0, 0) dx = \frac{1}{(4\pi Dt)^{1/2}} \exp \left[\frac{-(x - x_0)^2}{4Dt} \right] dx \quad (6)$$

for the probability that a solute molecule with x coordinate x_0 at time $t_0 = 0$ will have x coordinate between x and $x + dx$ at time t .⁹ Since diffusive motion is independent in each direction, the three-dimensional probability density equation is

$$P(x, y, z, t | x_0, y_0, z_0, 0) = (4\pi Dt)^{-3/2} \exp \left[-[(x - x_0)^2 + (y - y_0)^2 + (z - z_0)^2] / 4Dt \right] \quad (7)$$

It is convenient first to find the probability that a molecule

(1) For example, in L. D. Landau and E. M. Lifshitz, "Statistical Physics", Pergamon Press, London, 1953, pp 111–115.

(2) F. Reif, "Fundamentals of Statistical and Thermal Physics", McGraw-Hill, New York, 1965.

(3) M. v. Smoluchowski, *Phys. Z.*, 17, 557 (1916); *Kolloid Z.*, 18, 48 (1916).

(4) L. Onsager, *Phys. Rev.*, 38, 2265 (1931).

(5) B. J. Berne and R. Pecora, "Dynamic Light Scattering", Wiley, New York, 1976.

(6) R. M. Noyes and W. C. Gardiner, Jr., *J. Phys. Chem.*, preceding article in this issue.

(7) H. S. Carstow and J. C. Jaeger, "Conduction of Heat in Solids", 2nd ed, Oxford, 1959.

(8) W. Jost, "Diffusion in Solids, Liquids, Gases", Academic Press, New York, 1960.

(9) A. Einstein, *Ann. Phys.* (4), 17, 549 (1905).

starting with x coordinate somewhere in the range a, b —i.e., with $a < x_0 < b$ —is still within a, b at time t ; this is the integral of (6) over the range

$$P_x(\text{in}, t | x_0, 0) = \int_a^b (4\pi Dt)^{-1/2} \exp(-[x - x_0]^2/4Dt) dx \quad (8)$$

Scaling the x axis to $(4Dt)^{1/2}$ units and defining $a' = a/(4Dt)^{1/2}$ and $x_0' = x_0/(4Dt)^{1/2}$ leads straightforwardly to

$$P_x(\text{in}, t | x_0, 0) = \frac{1}{2} [\text{erf}(b' - x_0') - \text{erf}(a' - x_0')] \quad (9)$$

We require the average nonescaped probability. In general this would be

$$\langle P_x(\text{in}, t | \text{in}, 0) \rangle = \frac{1}{b-a} \int_a^b f(x_0) P_x(\text{in}, t | x_0, 0) dx \quad (10)$$

where $f(x_0)/(b-a)$ is a normalized distribution function giving the probability of starting between x_0 and $x_0 + dx_0$. By our basic assumption of the solute molecules having random starting locations, it is uniform and so $f(x_0)$ is set to unity. To make the integration of (10) simple, (9) can be converted to the complementary error function

$$P_x(\text{in}, t | x_0, 0) = \frac{1}{2} [\text{erfc}(a' - x_0') - \text{erfc}(b' - x_0')] \quad (11)$$

whereupon utilizing the first repeated integral of the error function¹⁰

$$i^1 \text{erfc } z = \int_z^\infty \text{erfc } t dt = e^{-z^2}/\pi^{1/2} - z \text{erfc } z \quad (12)$$

one obtains directly

$$\langle P_x(\text{in}, t | \text{in}, 0) \rangle = \text{erf } \beta - (1 - e^{-\beta^2})/\beta\pi^{1/2} \quad (13)$$

where

$$\beta = b' - a' = (b-a)/(4Dt)^{1/2} \quad (14)$$

(From (14) we immediately have the average escaped probability in the x coordinate alone

$$\langle P_x(\text{out}, t | \text{in}, 0) \rangle = 1 - \langle P_x(\text{in}, t | \text{in}, 0) \rangle = \text{erfc } \beta + (1 - e^{-\beta^2})/\beta\pi^{1/2} \quad (15)$$

which is also Smoluchowski's result for escape from an infinite slab.)

For the three-dimensional situation, the joint probability of the molecule having at time t the coordinates x, y, z within the ranges $a_x < x < b_x, a_y < y < b_y, a_z < z < b_z$ gives the average probability of the molecule remaining within the Cartesian volume $v = (b_x - a_x)(b_y - a_y)(b_z - a_z)$. This joint probability is the product of the three corresponding forms of (15)

$$\langle P(v, t | v, 0) \rangle = \langle P_x(\text{in}, t | \text{in}, 0) \rangle \langle P_y(\text{in}, t | \text{in}, 0) \rangle \times \langle P_z(\text{in}, t | \text{in}, 0) \rangle = \prod_{i \in x, y, z} [\text{erf } \beta_i - (1 - e^{-\beta_i^2})/\beta_i\pi^{1/2}] \quad (16)$$

If the molecule is not within v , it must be within $V-v$, so by completeness

$$\langle P(V-v, t | v, 0) \rangle = 1 - \langle P(v, t | v, 0) \rangle = 1 - \prod_{i \in x, y, z} [\text{erf } \beta_i - (1 - e^{-\beta_i^2})/\beta_i\pi^{1/2}] \quad (17)$$

Equation 17 is the desired general result for use with (2) and (3) to compute the time evolution of concentration fluctuations in three-dimensional Cartesian geometry.

For the special case of a cubic box, $\beta_x = \beta_y = \beta_z = \beta$ and

$$\langle P(V-v, t | v, 0) \rangle = 1 - [\text{erf } \beta - (1 - e^{-\beta^2})/\beta\pi^{1/2}]^3 \quad (18)$$

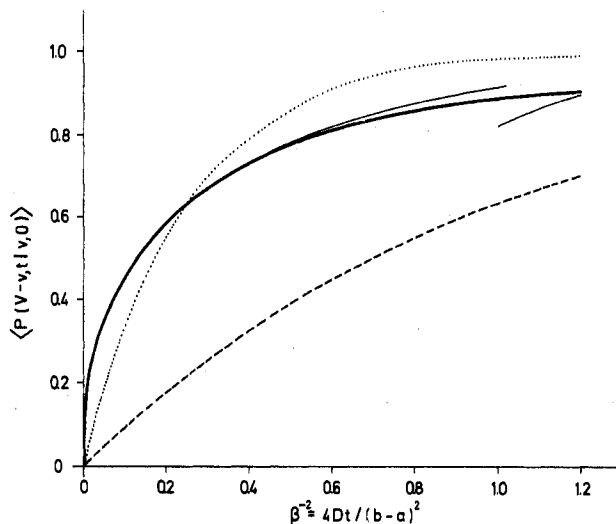


Figure 1. Escaped probability function for cubic geometry. The fine lines indicate the asymptotic forms, (19) and (20), the dashed line is for exponential decay according to $1 - e^{-t/\tau}$, $\tau = (b-a)^2/4D$, and the dotted line is for exponential decay with $\tau = (b-a)^2/D$.

It is a universal function of time, scaled as $\beta^2 = 4Dt/(b-a)^2$, (cf. eq 14) shown in Figure 1. Equation 18 is remarkably well described by the asymptotic forms

$$\langle P(V-v, t | v, 0) \rangle \simeq 1 - (1 - 1/\beta\pi^{1/2})^3 \quad (19)$$

for large β (short time) and

$$\langle P(V-v, t | v, 0) \rangle \simeq 1 - (\beta/\pi^{1/2})^3 \quad (20)$$

for small β (long time). Equation 19 is accurate to better than 3% for $\beta > 1.0$, better than 1% for $\beta > 1.5$, and better than 1 ppt for $\beta > 2.0$. Equation 20 is accurate to better than 8% for $\beta < 1.0$, better than 1% for $\beta < 0.6$, and better than 1 ppt for $\beta < 0.4$.

We can compare (18) with the simple t_D estimate for cubic geometry derived earlier,⁶ namely, $t_D = 5\lambda^2/48D = 5(b-a)^2/48D$. The corresponding value of β is $\lambda(4t_D D)^{-1/2} = (12/5)^{1/2} = 1.55$ (eq 14), for which $\langle P(V-v, t | v, 0) \rangle$ is 0.737. A fluctuation δn_i decreases in cubic geometry to 0.737 δn_i , on the average, in the time t_D that was used previously to characterize the dissipation of concentration fluctuations.

Solution in Spherical Geometry

The sum of squares appearing in the exponent of (7) has the meaning of the squared magnitude of the vector from x, y, z to x_0, y_0, z_0 , which is in spherical geometry $|\mathbf{r} - \mathbf{r}_0|^2$, where \mathbf{r}_0 is the vector locating the solute molecule at time $t_0 = 0$ and \mathbf{r} is the vector locating it at time t . The Brownian motion equation describing the diffusive motion from \mathbf{r}_0 to \mathbf{r} is thus

$$P(r, \theta, \phi, t | r_0, \theta_0, \phi_0, 0) r^2 \sin \theta d\phi d\theta dr = (4\pi Dt)^{-3/2} \exp[-|\mathbf{r} - \mathbf{r}_0|^2/4Dt] r^2 \sin \theta d\phi d\theta dr \quad (21)$$

Equation 21 provides the probability that a particle which starts at \mathbf{r}_0 will move to a volume element located at \mathbf{r} after time t . To obtain the total probability that a molecule which starts at \mathbf{r}_0 will at time t still be somewhere within a sphere of radius μ centered at the origin, we integrate over that sphere to obtain after straightforward substitutions and integrating by parts

$$P(v, t | r_0, 0) = \frac{1}{2\pi^{1/2} r_0} \{ \exp[-(\mu' + r_0')^2] - \exp[-(\mu' - r_0')^2] + \frac{1}{2} [\text{erf}(\mu' + r_0') + \text{erf}(\mu' - r_0')] \} \quad (22)$$

(10) M. Abramowitz and I. A. Stegun, "Handbook of Mathematical Functions", Dover, New York, 1965, Section 72.

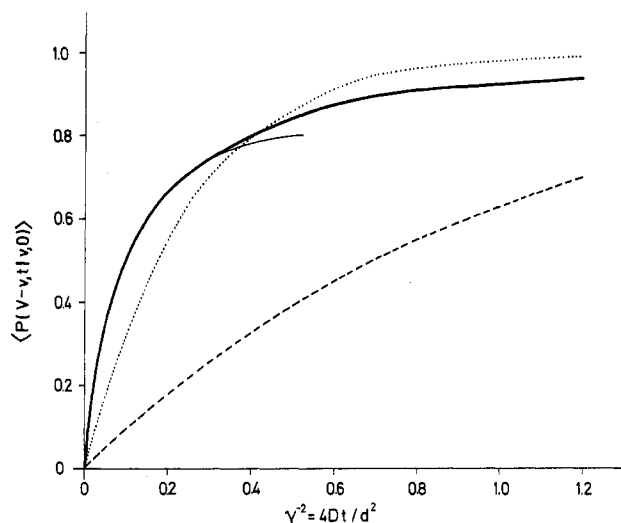


Figure 2. Escaped probability function for spherical geometry. The fine line indicates the asymptotic form (27), the dashed line is for exponential decay with $\tau = d^2/4D$, and the dotted line is for exponential decay with $\tau = d^2/D$.

where $r_0' = r_0/(4Dt)^{1/2}$, and $\mu' = \mu/(4Dt)^{1/2}$.

Equation 22 provides the time evolution of the probability that a given molecule initially r_0 away from the origin is also within μ of the origin at the time t . To obtain the average nonescaped probability for all values of r_0 , we require in analogy to (10) the normalized weighting function

$$f(r_0) dr_0 = (3r_0^2/\mu^3) dr_0 = (3r_0'^2/\mu'^3) dr_0' \quad (23)$$

corresponding to a uniform probability of r_0 locating a solute molecule within a volume element anywhere inside the sphere. Then the average nonescaped probability density is given by

$$\langle P(v, t | v, 0) \rangle = \int_0^\mu (3r_0'^2/\mu'^3) \left\{ \frac{1}{2\pi^{1/2}r_0'} [\exp[-(\mu' + r_0')^2] - \exp[-(\mu' - r_0')^2]] + \frac{1}{2} [\text{erf}(\mu' + r_0') + \text{erf}(\mu' - r_0')] \right\} dr_0' \quad (24)$$

which integrates tediously but straightforwardly to

$$\langle P(v, t | v, 0) \rangle = \text{erf } \gamma + [(2/\gamma^2 - 1)(1 - e^{-\gamma^2}) - 2]/\gamma\pi^{1/2} \quad (25)$$

where $\gamma = 2\mu' = 2\mu/(4Dt)^{1/2} = d/(4Dt)^{1/2}$ is the diameter d scaled by $(4Dt)^{1/2}$. For the average escaped probability then

$$\langle P(V - v, t | v, 0) \rangle = 1 - \langle P(v, t | v, 0) \rangle = 1 - \text{erf } \gamma - [(2/\gamma^2 - 1)(1 - e^{-\gamma^2}) - 2]/\gamma\pi^{1/2} \quad (26)$$

which is shown as function of scaled time in Figure 2. For large γ (short time) the asymptotic form

$$\langle P(V - v, t | v, 0) \rangle \simeq (3 - 2/\gamma^2)/\gamma\pi^{1/2} \quad (27)$$

is useful, as it describes the first 75% of the dissipation (for $\gamma > 1.8$) to better than 5 ppt. The series expansions required to obtain a small- γ result converge too slowly to provide a useful formula.

Our earlier estimate⁶ for the characteristic dissipation time of concentration fluctuations in spherical geometry

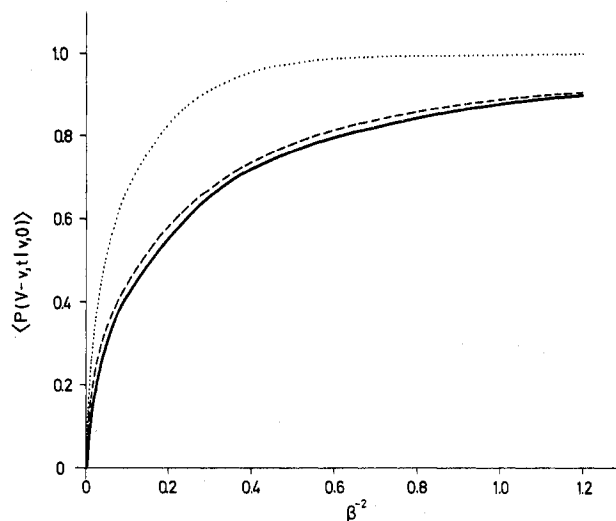


Figure 3. Escaped probability functions for a sphere (solid line) and for a cube (dashed line) of equal volume. The dotted line shows the rate for diffusive loss from a sphere of the same diameter under the radiative boundary condition, for which reentry does not occur.

$t_D = 7d^2/96D$ corresponds to $\gamma = 1.852$ and $\langle P(V - v, t | v, 0) \rangle = 0.741$, very nearly the same as the 0.737 value obtained above for cubic geometry.

We wish to compare the rate of diffusive loss of molecules from a sphere to that from a cube of equal volume. The diameter of such a sphere is then related to the side length of the cube by $d = (6/\pi)^{1/3} \lambda$. Scaling the sphere size to the cube size this way then provides the purely geometrical escaped probability comparison shown in Figure 3.

The classical diffusion equation for spherical geometry has been solved for the escape of molecules from a sphere into a vacuum, i.e., with the boundary condition that the concentration is held at zero outside the sphere, the initial concentration within, c_i , being uniform.¹¹ The average concentration \bar{c} is given by

$$\bar{c} = c_i \left(\frac{6}{\pi^2} \right) \sum_{k=1}^{\infty} \frac{1}{k^2} \exp \left[\frac{-k^2 \pi^2 D t}{\mu^2} \right] \quad (28)$$

and the average escaped probability becomes³

$$\langle P(V - v, t | v, 0) \rangle = 1 - \bar{c}/c_i = 1 - \frac{6}{\pi^2} \sum_{k=1}^{\infty} \frac{1}{k^2} \exp \left[\frac{-k^2 \pi^2 D t}{\mu^2} \right] \quad (29)$$

This solution, again with the diameter scaled to permit comparison with a cube of equal volume, is also shown in Figure 3.

Discussion

Our original motivation was to provide exact $\langle P(V - v, t | v, 0) \rangle$ functions for scaling diffusive dissipation of concentration fluctuations to rates of chemical reaction. The result, i.e., eq 18 and 26 and their asymptotic forms eq 19, 20, and 28, serve this intended function. As the numerical results show, the simple estimates based upon average diffusion distances were not misleading. It would have been misleading to use the radiative boundary condition solution (29) for comparison, for it is three times faster than the solution (30) of the real dissipation equation. [The difference between (29) and (26), incidentally, represents the probability as function of time that molecules

(11) H. Dünwald and C. Wagner, *Z. Phys. Chem. B* 24, 53 (1934).

which left the sphere, one or more times, returned and then left again to be outside at time t .] But correct accounting for the characteristic difference between diffusion and reaction rates, in that the former are initially infinite, as well as going from an order-of-magnitude estimate to exact solutions have both left our original conclusions about relative rates unchanged.

Equations 18 and 26 also serve as the three-dimensional equivalents of Smoluchowski's one- and two-dimensional results (4) and (5). They can be applied in molecular dynamics computations as measures of D .¹²

More striking than the difference between radiative and diffusive boundary conditions is the difference between the solutions for $\langle P(V - v, t | v, 0) \rangle$ and the corresponding

exponential relaxation equations [Figures 1 and 2]. As an approximation, exponential relaxation with $\tau = d^2/D$ (spherical case) or $\tau = (b - a)^2/D$ (cubic case) does provide a rough guide for the overall course of the dissipation of concentration fluctuations. The mathematical form is, however, very wrong, and the behavior at short and long times is far from the truth. It is clearly quite incorrect to infer from the extremely small magnitudes of concentration fluctuations in macroscopic systems that their dissipation can be described as exponential relaxation, as one would derive by setting $\langle P(V - v, t | v, t_0) v, t_0 \rangle = \text{constant}$ and $\langle \delta n \rangle / (\langle n \rangle - n) \simeq \langle d \ln n / dt \rangle$ in (2). "Linearization" of the dissipation process has no physical basis.

Acknowledgment. This work was undertaken during the tenure of a U.S. Senior Scientist Award from the Alexander von Humboldt-Stiftung. We thank M. Eigen for the hospitality of this institute.

(12) A. Rahman in "Statistical Mechanics—New Concepts, New Problems, New Applications", S. A. Rice, K. F. Freed, and J. C. Light, Eds., Chicago University Press, Chicago, 1972.

Thermodynamics of Solute-Solute Hydrophobic Interaction. Interactions of Hydrophobic Species with Lipid

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The interactions between hydrophobic species and lipid aqueous dispersions were investigated by highly sensitive differential scanning microcalorimetry in order to further examine the solute-solute hydrophobic interaction. The hydrophobic species used were quaternary ammonium salts, including tetraalkylammonium salts and azoniaspiroalkane salts, and cyclohexanol and some other alcohols. The order of the ability of these salts and alcohols to lower the phase-transition temperature and to affect the enthalpy (ΔH) and the entropy (ΔS) of transition of aqueous dispersions of 1,2-dipalmitoyl-L-3-glycerolphosphatidylcholine (DPPC) from gel to liquid-crystalline phase was parallel with those of these salts and alcohols for hydrophobic hydration and hydrophobic interaction with protein. As these salts or alcohols were added, the changes in ΔH and ΔG of the melting from gel to liquid-crystalline phase were of opposite sign: that is, $\Delta H > 0$ and $\Delta G < 0$ for water-structure makers and $\Delta H < 0$ and $\Delta G > 0$ for water-structure breakers. The observed opposition in sign for ΔH and ΔG is in parallel with a previously reported characteristic of solute-solute hydrophobic interaction. The modern ideas of hydrophobic interaction could help in the interpretation of the physicochemical nature of the phase-transition process of aqueous dispersions of DPPC.

Introduction

In our previous studies¹⁻³ on solute-solute hydrophobic interaction of protein with hydrophobic species, quaternary ammonium salts, including tetraalkylammonium and azoniaspiroalkane salts, were used to investigate the effects of alkyl chain length and of geometric configuration in alkyl-substituted quaternary ammonium salts on their interaction with protein. Tetraalkylammonium and azoniaspiroalkane salts contain linear and cyclic alkyl groups on quaternary ammonium ions, respectively. We found that a change in hydrophobicity, due to the changes in alkyl chain length and molecular shape, is responsible for a change in solute-solute hydrophobic interaction^{1,2} analogous to the previously reported⁴⁻⁷ solute-solvent

hydrophobic hydration. Formation of cyclic groups in these ions considerably weakens their ability for hydrophobic interaction with protein.

We also interacted protein with a variety of alcohols having known free-energy and enthalpy pairwise-interaction coefficients.^{8,9} These alcohols were found to have the same order of abilities for solute-solute hydrophobic interaction with protein and for self-pairwise interaction between alcohol molecules. Thus the stronger the tendency of an alcohol molecule for pairwise interaction between its molecules, the greater its ability for hydrophobic interaction with protein.

Cyclohexanol is one of the most hydrophobic species, having a reasonably good solubility in water.⁸ Comparison of thermodynamic parameters for the interactions of cyclohexanol and quaternary ammonium salts with protein

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