Diffusion in gels

Alan H. Muhr and John M. V. Blanshard
Food Science Laboratories, Department of Applied Biochemistry and Food Science, Nottingham University, Sutton Bonington, Loughborough, Leicestershire, UK
(*Received* 7 *August* 1981)

The diffusion of solutes in gels is comprehensively reviewed. Because it has been a source of confusion, precise definitions of the gel diffusion coefficient are presented and discussed. Theories as to the effect of the gel substance on the course of diffusion are critically evaluated. These include the obstruction effect, hydrodynamic drag and other frictional couplings, alteration of solvent properties and (for homogeneous gels) the free volume theory. A large proportion of the data on diffusion in gels to be found in the literature is displayed, with the exception of those systems where binding of the solute is a major factor. The success of the theories in accounting for these results is examined. It is concluded that for heterogeneous gels the obstruction effect is prevalent, for organic solvent–polymer systems the free volume theory has had some success while diffusion of both macromolecules and micromolecular solutes in homogeneous gels is not well understood and deserves more experimental effort.

Keywords Polymer gels; diffusion coefficients; solute diffusion; obstruction effect; hydrodynamic drag; frictional couplings; tortuosity; free volume; activation energy

INTRODUCTION

While diffusion in polymer gels and solutions is of direct interest for its own sake in a wide variety of fields, gels also provide a system in which diffusion may be easily studied without the hazard of convection, and from which it is often hoped that the free solution diffusivities can be inferred[1-6]. Other workers have studied diffusion in gels in order to evaluate gel structure[7-11].

Gels

Gels cover a spectrum from one phase or homogeneous dynamic solutions (where entropy of the mix is the chief factor responsible for retention of the solvent, and 'pores' are neither constant in size nor location) to two phase or heterogeneous rigid porous structures (where capillary forces are responsible for solvent retention). For this reason results and theories for diffusion in polymer solutions and porous media will be included in this review.

From a knowledge of the nature of the crosslinks or junction zones it is possible to get some idea of the fraction of polymer which is associated with these semi-permanent structures, and hence roughly where in the spectrum a particular gel lies. Thus for aqueous gels, polyacrylamide gels are expected to be fairly homogeneous[12,13]; *i*-carrageenan, κ-carrageenan, furcellaran and agarose form a series of gels of increasingly heterogeneous nature[14]; calcium alginate gels become progressively more heterogeneous as more Ca^{2+} ions are added during preparation, thus increasing the number of polysaccharide chains participating in the junction zones[15]. However, much more uncertainty surrounds the actual geometry of the semi-permanent structures. A further complication arises for gels which might be expected to be homogeneous, but which at sufficiently high water content and degree of crosslinking suffer phase separation on gelation from the monomer or polymer solution. This results in a mixed structure of homogeneous fully swollen regions of gel and pockets of solvent, and is often accompanied by syneresis[10]. Direct observation by electron microscopy has been attempted for silica and gelatin gels[16], gelatin gels[17], alginate gels[18], poly(*N*-alkylacrylate) gels[19], and various protein gels[20], but it is uncertain how much of the observed structure is an artefact of sample preparation.

In formulating theories of diffusion in gels, it is usually necessary to have an idealized picture of the structure. One widely used picture due to Ogston[21] treats gels as random networks of fibres; their radius is the only important structural parameter. It is considered that randomness includes the possibility of lack of rigidity so that no distinction need be drawn between gels and solutions[22]. This model has also been extended to include disc-shaped and spherical particles of gel substance as well as fibres[23].

Factors affecting diffusion in gels

The fractional decrease D/D_0 in the rate of diffusion of a small solute on the addition of a polymer to the solvent is often at least an order of magnitude less than the fractional increase η/η_0 in macroscopic viscosity[24]. This result would at first sight appear to be at variance with the classical hydrodynamic theory of diffusion, which gives the diffusion coefficient D of a trace impurity as[25]:

$$D = kT4\pi\eta r$$

where k is the Boltzmann constant, T the absolute temperature, η the medium viscosity and r the radius of the diffusing molecule. However, for a diffusing solute of molecular size considerably less than that of the polymer, a more appropriate application of this theory would treat the polymer–solvent system as a continuum in which large objects are suspended. As yet no complete hydrodynamic treatment of the motion of small spheres through such a system has been developed[26]. In addition to the hydrodynamic interactions (numbers 1 and 2

0032-3861/82/071012-15$03.00

below) there may be more specific interactions between solute, solvent and polymer; alternatively an entirely different model for diffusion, the free volume theory, could be applied. Thus the polymer may influence solute diffusion in any (or all) of the following four ways:

(1) *The obstruction effect.* The presence of impenetrable, slow moving polymer molecules leads to an increase in the path length for diffusion.

(2) *Increased hydrodynamic drag.* The proximity of the slow moving polymer–solvent interface leads to an increased hydrodynamic drag on the moving solute molecules.

(3) *Alteration of solvent properties.* The presence of the polymer may alter properties of the solvent such as intermolecular spacing.

(4) *Polymer involvement.* Shearing of polymer–solvent and polymer–solute bonds and bending of polymer chains may occur with significant frequency during solute diffusion. In addition, the polymer content of the medium in which diffusion occurs may have significant effect on its free volume.

Before embarking on a detailed discussion of these ideas and how successfully they explain results, it is necessary to clarify some issues which relate to definitions and scope.

Binding of the solute

Firstly, one important way in which the gel substance may affect diffusion is by binding the solute. The mobilities of bound and free solutes may then be characterized by different diffusion coefficients, D_{bound} and D_{free}, so that Fick's first law becomes:

$$J = -D_{bound}(\partial C_{bound}/\partial x) - D_{free}(\partial C_{free}/\partial x)$$

If the relationship between C_{bound} and C_{free}, and the values of D_{bound} and D_{free} are known, it may then be possible to predict the measured diffusion coefficient D defined by

$$J = -D\partial(C_{bound} + C_{free})/\partial x$$

The simplest case of binding occurs if $D_{bound} = 0$ and $C_{bound} = \alpha\ (C_{bound} + C_{free})$, where α is independent of concentration and position. It follows that $D = (1-\alpha)\, D_{free}$, which is the result of Wang[27] for diffusion of labelled water in a system in which the fraction α of water is bound and immobile, but exchanges very rapidly with the free water. This result applies to both steady state and transient diffusion, provided D is defined in terms of total concentration per unit gel volume.

More complicated cases have been discussed by Paul and Kemp[28] and Paul and Koros[29]. A widely occurring situation is that of the diffusion of counterions in polyelectrolyte gels or ion-exchangers[4,30–33] where the binding of the solute at a limited number of sites results in D being concentration dependent even when D_0 is not.

As the binding will depend on the specific nature of the system, it seems more fruitful to concentrate attention below on more general features.

Swelling and frames of reference

A problem characteristic of diffusion in gels is that the gel volume may not remain constant throughout the experiment. This may occur because the gel has not reached an equilibrium degree of swelling before exposure to a solution from which (or into which) solute diffusion takes place—the cause of such swelling may be removed either by first equilibrating the gel in the solvent for a prolonged period of time[13,34] or by setting up the solute concentration gradient entirely within the gel, thus removing the need for an external solution[31]. However, the progress of diffusion may itself cause swelling, and this case will now be considered in some detail.

Clearly all systems of interest here have at least three components—polymer, solvent and solute. In such systems a component, although itself distributed uniformly, may flow due to the existence of concentration gradients of the other components. Such flow may be caused either by frictional coupling (the diffusional flows of the other components exerting a net driving force) or by thermodynamic coupling (the chemical potential of the component, which is the driving force for diffusion, will generally depend on the concentrations of the other components)[35]. Frictional coupling could cause heterogeneous gels to shrink or swell during diffusion, while homogeneous gels are subject to both sorts of coupling. In addition, it has been suggested that in the course of diffusion in solutions pressure gradients arise which are relieved by a 'bulk flow' of the solution, and that such flow can be detected by the motion of marker particles[36]. The gel matrix may function in this capacity. It has been variously stated that the bulk velocity is the local mass-fixed velocity[37,38], the local volume-fixed velocity[39] or indeed is distinct from any of the customarily used reference velocities for diffusion[36]. It has been noted, however, that the local mass-fixed, volume-fixed, mole-fixed and solvent-fixed velocities differ only when there is relative motion of solution components and that, in this case, the definition of 'bulk' or hydrodynamic velocity is only a matter of convention (usually the volume fixed velocity is chosen), even though there is a natural relationship) the equation of motion) between the pressure gradient and the mass-fixed velocity[40]. In practice, any effect of bulk flow on marker motion has been masked by frictional or thermodynamic coupling in the few systems which have been studied[38,41,42].

If the coefficient of diffusion in the gel (D) is to be compared to the coefficient of diffusion in the absence of the gel matrix (D_0) it is best, therefore, to use a frame of reference independent of possible motions of the gel matrix. If the solute concentration is very small, all the usual frames of reference become identical and swelling of the gel due to the progress of diffusion will be negligible; otherwise the various defining frames of reference yield different values of D which, however, may readily be interconverted[43]. The cell reference frame is the most commonly used, and is equivalent to the local volume-fixed frame except when there is a volume change on mixing, in which case the discrepancy is negligible provided the concentration differences are very small[40,44].

Solvent tracer diffusion and mutual diffusion

An interesting special case occurs when the solute is a labelled form of solvent, D_0 then being the self diffusion coefficient of the solvent (which will be denoted D_0^*) while D is termed the intradiffusion coefficient of the solvent in the gel (and will be denoted by D^*). In conventional diffusion experiments the labelling of the solvent is

generally achieved with an isotope while in n.m.r. diffusion experiments solvent molecules are labelled by means of nuclear spin. In such experiments it is possible that transport of the label may occur by a mechanism involving exchange as well as by the diffusional transport of the labelled molecule. An important case which has received attention is that of HTO. However, H_2O^{18}, HDO and HTO have been shown to be transported in ordinary water at almost the same rate[45], and in a cellulose acetate membrane of only 10% moisture content HTO and H_2O^{18} are transported, within experimental error at the same rate[46].

Apart from the above considerations, the diffusion of labelled solvent is no different in character from that of other small solvents. Nevertheless, some authors have attempted to infer the mutual diffusion coefficient (denoted here D_M) of the gel–solvent system from D^*. According to all known theories of diffusion,

$$\lim_{\phi \to 1} D_M = \lim_{\phi \to 1} D^*$$

where φ is the polymer volume fraction. A corresponding equality holds between $\lim_{\phi \to 0} D_M$ and the limiting polymer tracer diffusion coefficient, and the equalities hold for any two component system[47]. With less justification, relations between D_M and the intradiffusion coefficients of the components over the full composition have been proposed[36,48]; adaptations of these for polymer solutions are[48,49]

$$D_M = D^*(\partial \ln a_s / \partial \ln(1-\varphi))$$

and[36,50]

$$D_M = D^*\varphi(\partial \ln a_s / \partial \ln(1-\varphi))$$

where a_s is the activity of the solvent. In the system benzene–rubber the first of these formulae has been found adequate for $\varphi > 0.6$, but progressively underestimates D_M as φ decreases, predicting that at $\varphi = 0.05, D_M/D^* = 0.013$ whereas the measured value is $D_M/D^* = 0.056$; the second formula thus underestimates D_M to a much greater extent[42]. It can be taken, therefore, that apart from the case of φ close to unity[42,50] there is no generally reliable relationship between D^* and D_M. This is not surprising for gels, i.e. crosslinked polymer systems, since the gel matrix is unperturbed during solvent tracer diffusion whereas swelling is the hallmark of mutual diffusion, and the attendant strains may well give rise to anomalous effects[51,52]. Thus while there has been recent progress in the understanding of general features of mutual diffusion in polymer solutions[50], the kinetics of swelling of a gel are inevitably a specific property, and sometimes are even regarded as a phenomenon separate from diffusion[13].

Units of solute concentration and flux

Solute concentration may be defined as either the amount of solute per unit volume of gel (here denoted C_G), or the amount of solute per unit void volume (here denoted C_V). For porous media C_V is the more usual and appropriate measure, but in any case $C_G = (1-\varphi)C_V$. In general neither C_G nor C_V will be equal to the concentration of a solution in equilibrium with the gel (denoted here C_E), but are related to C_E by the partition coefficient K defined by $C_G = KC_E$. For non-adsorbed solutes, the usual approach to theoretical predictions of K is the geometric exclusion effect— the fractional void volume available for the centres of large solute molecules (here denoted $1-\Phi$) being less than the available for the centres of the smaller solvent molecules ($1-\varphi$), which can more closely approach the void walls. It follows that $C_G = (1-\Phi)C_E$, so that $K = 1-\Phi$. Such calculations require a specific model of gel structure [21,53,54] and for a given K can yield parameters related to the fineness of dispersion of the gel substance[55]. However, for known structure and pore size they have sometimes been found to be at variance with values of K determined experimentally[54]. Furthermore, low values of K have been found for inorganic salts in cellulose gels and polyacrylamide gel pointing to the existence of factors other than steric exclusion[56].

Frequently in diffusion experiments on gels, the experimentally measured concentrations are those of external solutions, and sometimes (especially for membranes) an effective diffusion coefficient (denoted D_{eff}) is defined by $J = -D_{\text{eff}}\dfrac{\Delta C_E}{\Delta X}$ where J is the flux per unit area of gel of thickness ΔX, which separates solutions differing in concentration by amount ΔC_E. It follows that $D_{\text{eff}} = KD$ where D is defined by $J = -D\dfrac{\Delta C_G}{\Delta X}$ (see *Figure* 1). While D_{eff} is of practical use, it is necessary to devise experiments from which K and D can be found independently for a more complete understanding[1,34,54], which unfortunately has not been done in some otherwise careful studies[9,53]. Furthermore, it should be noted that it has sometimes been tacitly assumed that $K = 1$, leading to errors in the calculation of the diffusion coefficient[7,57,58] or apparent failure of standard solutions of the diffusion equation[59]. These will become more significant with increase in polymer concentration, since (for unbound solutes) $K \leqslant 1-\varphi$. Further complications arise for non-uniformly crosslinked gels, where φ (and hence K) is an unknown function of position[56].

Reduced cross-sectional area for diffusion

If the solute is excluded from a volume fraction Φ of the system, then there is also a certain fraction of the area of any lamina across which transport cannot take place. Dumanski[60] gave $\Phi^{2/3}$ as the value of this fraction of area

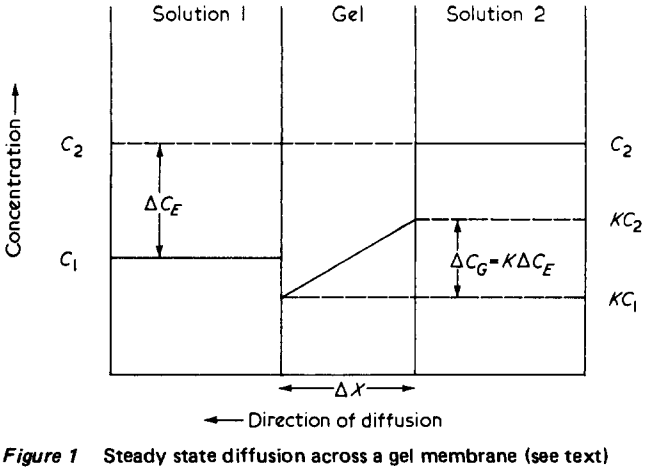

Figure 1 **Steady state diffusion across a gel membrane (see text)**

and claimed this to be the chief mechanism of reduction of the rate of diffusion by the colloid. However, the correct result is that the average reduction in cross-sectional area is equal to the volume fraction of obstacles (Φ), this being the principle of Delesse[61]. With this correction, the idea of reduced cross-sectional area for diffusion[57] and for electrophoretic transport[23] has been used more recently. Against this idea it has been pointed out that while the diffusive flux based on unit total area is $(1-\Phi)$ times the flux based on unit void area, so also is the concentration (and hence the concentration gradient) based on unit total volume $(1-\Phi)$ times the concentration based on unit void volume. Thus D, the ratio of flux to concentration gradient, is the same whether we define flux and concentration in terms of total area and volume or in terms of obstacle free area and volume, and is unaffected by reduction in cross-sectional area[62]. D_{eff} is, of course, reduced by the cross-sectional area effect as we see from the relation $D_{eff}=(1-\Phi)D$.

Fick's second law for gel diffusion

By the usual method of calculating the amounts diffusing into and out of an infinitesimal (but large with respect to the gel grain size!) section, Fick's second law can be derived for gel diffusion:

$$\frac{\partial C_G}{\partial t}=D\frac{\partial^2 C_G}{\partial x^2}$$

which is clearly also valid if C_G is replaced by C_V or C_E. It at once follows that in terms of D_{eff} Fick's second law assumes the unusual form:

$$K\frac{\partial C_E}{\partial t}=D_{eff}\frac{\partial^2 C_E}{\partial x^2}$$

This point was noticed by Satterfield *et al.*[54] (who unfortunately use the same symbol for D and for D_{eff}), Higuchi and Higuchi[63] (who refer to D_{eff} as the effective permeability) and Lauffer[1,64], but missed by Wang[27] who erroneously compared his measured D values (the solutions of Fick's second law in usual form) with theoretical D_{eff} values.

Range of polymer concentration

The value of φ has varied in the different systems experimentally studied over the whole range from 0 to 1. It is thus important to consider the regions in the range of φ in which theoretical viewpoints are to be expected to be valid. If the gel substance is coarsely dispersed, as in a porous solid, then the local environment of the solute and solvent molecules may be virtually independent of φ. However, in the case of a polymer solution (the extreme case of fine dispersion) solvent molecules will be isolated from each other at sufficiently high values of φ, resulting in quite different mechanisms of diffusion from those at low φ[49]. As an example, the test for the existence of pores in membranes devised by Thau *et al.*[46] will be considered. This test requires measurement of two permeabilities: the solvent tracer permeability which depends on the sum of solvent–membrane and solvent–solvent friction, and the hydraulic permeability which depends only on solvent–membrane friction. The relative importance of the friction factors in solvent tracer diffusion can thus be inferred, and the existence of large pores is concluded if solvent–solvent friction is much greater than solvent–membrane friction. However, significant solvent–solvent friction is inevitable at intermediate or low φ values ($\varphi \leqslant 0.75$), so the test is only helpful if φ is very high[65].

THEORETICAL APPROACHES

(1) *The obstruction effect*

Tortuosity. Frequently in the literature on porous media, or indeed for homogeneous membranes, the mean increase in path length due to obstructions is referred to as the 'tortuosity', here denoted θ. The concept of tortuosity also occurs in the study of flow through porous media, and a good review is provided by Carman[66]. If the medium is modelled as a bundle of capillaries of uniform cross-section, tortuously connecting the two surfaces across which a concentration gradient had been set up, it is easy to show that $D/D_0=\left(\frac{1}{\theta}\right)^2$. The square relationship arises because the concentration gradient along the capillaries is reduced by the same factor as the path length is increased. On considering a more realistic model, not only is difficulty experienced in the definition of tortuosity and in its subsequent calculation, but also in taking proper account of the variable cross-section of the void spaces and hence of the concentration gradient along the diffusion paths. Nevertheless, the above relationship between D/D_0 and tortuosity, although not rigorously true, has been retained[62,67]. Other workers[38,68] have with less justification preferred the relationship $D/D_0=\frac{1}{\theta}$. The complexity of the situation is illustrated by Boyack and Giddings[69] who, for the analogous case of electrical conductivity, include a 'constriction' factor as well as the $\left(\frac{1}{\theta}\right)^2$ factor. A rigorous solution of the problem, for steady state diffusion, would require the solution of Laplace's equation in the void spaces of the media, with appropriate boundary conditions on the surfaces. To an approximate degree, this approach has been applied to a range of systems and will now be discussed.

Laplace equation approach. Many expressions have been derived for steady state diffusion in a medium composed of immobile, impenetrable objects of volume fraction φ embedded in a uniformly permeable continuous phase. Mathematically, the problem is to solve $\nabla^2 C_V=0$ in the void space of a slab of the medium, with the boundary conditions that C_V takes the values C_1, C_2 at the faces and that only tangential diffusion can occur on the surfaces of the impenetrable objects. From a knowledge of C_V, J can be found by averaging $-D_0\nabla C_V$, and hence D_{eff} from $J=-D_{eff}\frac{\Delta C_E}{\Delta X}$. In the first instance the majority of expressions were derived many years ago for the mathematically analogous properties of electrical permittivity and conductivity (for example for the conductivity problem we need only replace C_V by potential, J by current density and D_0 by conductivity) and many reviews are available[70,71]. Most of these formulae treat the more general case of two phase systems in which both phases are penetrable but with different permeabilities.

It is interesting to note that the equation of Wang[27]

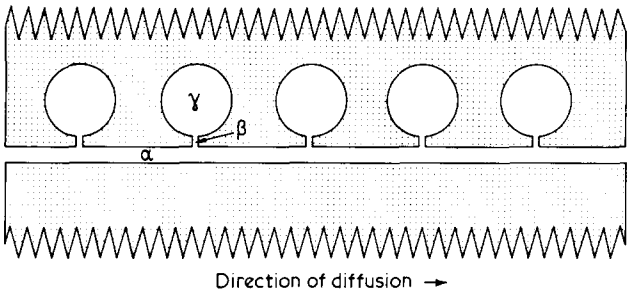

Figure 2 A porous medium in which non-steady state diffusion may not be described by the steady state diffusion coefficient (see text)

specifically for diffusion can be derived as a special case of Fricke's treatment[72] which was published thirty years earlier. Fricke's equation for a random suspension of impenetrable spheroids is

$$\frac{D_{\text{eff}}}{D_0} \simeq \frac{1-\varphi}{1+\varphi/x} \quad \text{or} \quad \frac{D}{D_0} \simeq \frac{1}{1+\varphi/x}$$

where $x=2$ for spheres, x approaches 0 in the limit for oblate spheroids and x approaches $\frac{3}{2}$ in the limit for prolate spheroids. The equation shows excellent agreement with conductivity data for dogs blood[72], with the volume concentration of red corpuscles (insulators) ranging from 10% to 90%. Hashin and Shtrikman[73] have shown that $\frac{1-\varphi}{1+\varphi/2}$ (often known as Maxwell's expression for D_{eff}/D_0 for spheres) is in fact an upper bound for D_{eff}/D_0 for any φ and for impenetrable objects of any shape.

All the formulae available refer to the steady state case, analysis of the non-steady state problem being extremely difficult. However, the value of D will be the same for non-steady state diffusion if the time for steady state attainment in a microscopic heterogeneous region is small compared to the time required for a unit change in concentration in that region[63]. For a two phase system with one phase impenetrable, this may not be the case if there is a highly non-uniform distribution of pore sizes, with significant volumes of the penetrable phase accessible only through very narrow pores. Such an idealized structure is shown in *Figure 2*. For steady state diffusion only pores of type α are important for transport, pore λ affecting D only through its influence on K. Provided it is small, the diameter of the β pore does not greatly affect steady state diffusion. In contrast, for non steady-state diffusion the influence of the size of the β pores on $\frac{\partial C}{\partial t}$ would be very great. However, for random suspensions of the types discussed above the distribution of pore sizes should be fairly regular, so that the formulae can with reasonable confidence be used for non-steady state diffusion.

A stochastic approach. When the 'impenetrable obstacles' are very small, with a size of a similar order of magnitude to the diffusing molecules, it seems unreasonable to use the above continuum picture. Mackie and Meares[67] used the lattice model for liquids, and pictured the polymer as blocking a fraction φ of sites. Diffusion of a solute (equal in size to the polymer segments) was considered to be restricted to the free sites. Making an approximate allowance for the existence of the polymer as chains with occasional crosslinks they derived an expression for the tortuosity:

$$\theta = \frac{1+\varphi}{1-\varphi}$$

whence $D/D_0 = \left(\frac{1-\varphi}{1+\varphi}\right)^2$

There is room for a more spohisticated treatment of the relative rates of motion of the components and of the degree of association or crosslinking of the polymer within the framework of this approach, especially if numerical methods of solution are employed. A simple application for a monomer occupying fraction φ of sites, whose motion is so rapid that distribution of sites may always be treated as locally random, yields $\theta = \frac{1}{1-\varphi}$ whence $D/D_0 = (1-\varphi)^2$. For immobile obstacles θ would be rather greater. The approach is, however, limited both by the treatment of polymer segments and solute molecules as equal in size, the rather artificial lattice model, and the use of the doubtful relationship $D/D_0 = \left(\frac{1}{\theta}\right)^2$.

The rather greater reduction in diffusion rate predicted by this approach compared to that of the Laplace equation is connected with the fine degree of dispersion of the obstacles. The volume of the obstacles is effectively increased by a shell of the thickness of the solute radius r. Thus φ in Fricke's equation should be replaced[1,64] by Φ. It is not clear, however, which approach involves the more drastic idealizations.

A stochastic approach for large solute molecules. A significant number of the gaps between the obstacles may be insufficient to allow the passage of very large diffusing molecules. In these circumstances, replacement of φ in Fricke's formula with Φ is no longer valid, and indeed Φ is no longer easily calculated as the overlap of the excluded volumes of the individual obstacles needs to be considered. For randomly oriented straight fibres, Ogston[21] has derived the expression

$$\Phi = 1 - \exp[-\pi L(r+\rho)^2]$$

where L is the length of fibre per unit volume and ρ is the fibre radius. This formula may be compared to the nonoverlap situation:

$$\Phi = \pi(r+\rho)^2 L$$

The root-mean-square radius of spherical spaces in a random network of straight fibres has been shown to be $(\pi L)^{-\frac{1}{2}} - \rho$. For $\rho = 0.5$ nm, this gives 4.5 nm for $\varphi = 0.01$ and 1.1 nm for $\varphi = 0.1$. For solute molecules of this order of size the chief cause for reduction of the diffusion rate will be the limited number of spaces available in the network, if the network is unperturbed by the diffusing molecules. From this point of view Ogston *et al.*[62] have derived the expression

$$D/D_0 = \exp[-(\pi L)^{\frac{1}{2}}(r+\rho)] = \exp[-\varphi^{\frac{1}{2}}(r+\rho)/\rho]$$

Like the Fricke equation with φ replaced by Φ, this expression has a parameter (ρ or L) related to the fineness of dispersion of the gel substance; ρ may be determined from comparison of measured partition coefficients with the Ogston expression for Φ. The values of ρ so obtained[55] appear reasonable, the discrepancy of ρ with the radius of a single polymer chain[74] being satisfactorily explained as due to chain association.

Since the network is not considered to be perturbed by the diffusing molecules, the theory applies equally to gels or polymer solutions.

(2) *The effect of increased hydrodynamic drag*

The idea that the proximity of the stationary gel substance results in an enhanced frictional drag on the diffusing molecules was first introduced by Friedman and Kraemer[7], who treated gels as having cylindrical pores. The decreased rate of diffusion is obtained from Faxen's solution to the problem of the fall of bodies in pipes, which gives[75]

$$D/D_0 = 1 - 2.1r/R$$

to first order in r/R, where R is the pipe radius. In a fairly well characterized porous medium ($R = 1.6$ nm) the more exact solution of Haberman and Sayre was found to give the wrong functional dependence of D/D_0 on r/R, although the predicted and observed effects were of similar magnitude[54]. Possible reasons for the failure of the equations are the idealized nature of the pore geometry used in the model, and/or a breakdown of the continuum assumption in the pores. As gels are far less well characterized and probably more random in structure, the treatment of Friedman and Kraemer is best regarded as a mathematical convenience rather than a physical picture.

Broersma[76] has developed expressions for the frictional drag on spherical particles moving in a medium in which the viscosity varies with distance from the particles. For the case of a solvent molecule in a slurry or solution, the viscosity is considered to increase from the solvent viscosity η_0 at the molecule, to the bulk viscosity η at ∞. This leads to an approximate expression $D_0/D = 1 + 0.3(\eta/\eta_0 - 1)$. While not directly applicable to gels, the theory is interesting and suggestive.

Thus there is no realistic quantitative theory available. Furthermore, tthe hydrodynamic drag effect is not the only way in which a dependence of D on r can arise, as has sometimes been supposed[7,54], since the path length may also vary with solute size. Some independent insight into the significance of the drag effect can, however, be obtained from rotational diffusion measurements, which will be discussed in the next section.

(3) *Alteration of solvent properties*

Friedman and Kraemer[7] again introduced the idea that the viscosity of the solvent present in a gel may differ from the viscosity of the bulk solvent. While this would affect D, it is difficult to get an independent method to assess its significance. Friedman and Kraemer considered the change in solvent viscosity to be independent of φ, so that it could be found from $\lim_{\phi \to 0} D/D_0$. This appears excessively simple, and furthermore the results of Friedman and Kraemer are the only ones which have the doubtful distinction of not extrapolating to $D = D_0$ at $\varphi = 0$. Clough *et al.*[77] claimed that the alteration of solvent viscosity is the principal factor in reducing the rate of solute diffusion. They took the limiting viscosity at high shear rate of a polymer solution (or slurry) to be the solvent viscosity in the solution; using this method the viscosity of water in a 1% CMC solution was found to be enhanced by a factor of 3.4. Osmers and Metzner[24] also argued that the principal influence of the polymer on diffusion in dilute polymer solutions is caused by the alteration of solvent properties—in particular, the solvent intermolecular spacing which they expressed as a function of the excess volume of mixing of the polymer and solvent. The viscosity of solvent in the solution was then equated with that of the pure solvent at a temperature such that the intermolecular spacing was the same as that given by their expression. The viscosity of water in a 1% CMC solution was in this way found to be enhanced by a factor of only 1.08. This more modest alteration of solvent viscosity, predicting $D/D_0 = \frac{1}{1.08}$ in the absence of other factors, is in much better agreement with the majority of experimental results for diffusion, although very low rates of diffusion of oxygen in CMC solutions have been reported.[78]

Rotational diffusion, being free of the requirement of hole formation or circumvention of obstacles, is considered to be a closer reflection of 'microscopic viscosity' than translational diffusion. However, rotational diffusion studies still cannot distinguish between direct or hydrodynamically coupled friction with the polymer and increased 'structural viscosity' of the solvent. Fluorescence depolarization studies of the rotational diffusion of fluorescein have shown that the microscopic viscosities of aqueous hydroxyethyl cellulose and polyacrylamide solutions[79] and hydroxyethyl cellulose gels[80], while considerably greater than that of water, are consistent with a much smaller effect than that claimed by Clough *et al.*[77] for CMC solutions. Even smaller effects have been observed in studies of the rotational diffusion of serum albumin in dextran[81] and hyaluronic acid[82] solutions. It is interesting to note that rotational diffusion is insensitive to the degree of polymerization[79,81] and is not greatly changed during the gelation of agar, gelatin and silica gels[83].

The existence of more than one state (bulk or bound) for solvent molecules has made interpretation of n.m.r. relaxation times too difficult to be sensitive to the finer details of solvent properties in gels, although it has been indicated that the bulk water in aqueous gels is not very different from pure water[84] in spite of earlier conjectures to the contrary.

It thus seems reasonable to assume that solvent properties are not significantly altered by the presence of the polymer unless diffusion results cannot otherwise be explained. In this spirit, the enhanced diffusion rates found in some polymer solutions were explained by alteration of solvent structure[85]. However, doubt has been cast on most of the experimental results indicating enhanced diffusion rates in polymer solutions[86,87]. Nevertheless, the water intra-diffusion coefficient has been found to be enhanced in certain electrolyte solutions (by as much as 28% for 4 molar KI solution at 10°C), so that at least for these systems the structure breaking effect of the ions appears to have a significant effect on diffusion[88].

(4) *Polymer involvement*

In order to make a diffusive jump, a molecule must attain sufficient energy to overcome attractive forces holding it to its neighbours and also an empty site must be available into which it can jump. The former is considered to be the rate controlling process in the Eyring rate theory of diffusion[89], while the free volume theory treats the latter as rate determining[90]. The relative importance of the two processes in viscous flow has been assessed for a variety of liquids[91]. While many solvents are borderline, broadly speaking flow in polymers and van der Waals liquids is free volume limited, while hydrogen bonded liquids are energy limited (except at low temperature where flow becomes free volume limited)[91]. These conclusions should also apply to diffusion. Both theories yield expressions of approximate Arrhenius form for the temperature dependence for diffusion at constant pressure.

For porous gels, diffusion of small molecules will take place in the solvent phase, so that (if the solvent is not altered by the gel substance) it is anticipated that the Arrhenius or apparent activation energy E (defined by $E=-R\frac{\partial \ln D}{\partial 1/T}$, where R is the gas constant) will be unaffected by the presence of the gel substance. For homogeneous gels the medium in which diffusion takes place becomes progressively more unlike the solvent as φ increases, so that a corresponding progressive change in E is to be anticipated, whether the diffusion is free volume controlled or activated. For example, as φ increases, diffusion will require increasingly frequent shearing of polymer–solute and polymer–solvent bonds. In addition, the solute molecules will sometimes be trapped in 'cages' of polymer molecules, so that D will become increasingly dependent on the mobility of the polymer segments, resulting in a greater apparent activation energy[92].

Recently a picture of molecular sieving processes has begun to evolve in which the retardation of large molecules is governed by the kinetics of distortion of the network, rather than by its geometry. This is in contrast to the theory of Ogston *et al.*[62], which was developed for sedimentation as well as diffusion. So far the new picture has only been applied to sedimentation[93] and gel electrophoresis[94]; for free diffusion the forces acting on the migrating molecules are perhaps insufficient to distort the network. Unfortunately the only study of the temperature dependence of a molecular sieving property seems to be that reported by Ogston *et al.*[62], showing no change in temperature dependence of sedimentation rate on adding a polymer to the solution, thus supporting their model.

The Eyring rate theory approach. According to this theory, an absolute calculation of the rate of diffusion of a trace species in a liquid can be made from the equation

$$D=\lambda^2 \underline{k}$$

where λ is the jump distance and $\underline{k}$ is the jump rate. If the transition (i.e. activated) state differs from the normal state only in having one less degree of freedom of translational motion, then the rate theory gives[89]:

$$\underline{k}=kT(2\pi mkT)^{-\frac{1}{2}}V_f^{\frac{1}{3}}\exp(-\varepsilon/kT)$$

where m is the mass of the diffusing solute (more correctly, the reduced mass of the solute–solvent pair), V_f is the average free volume available for each diffusing molecule and ε is the difference in energy per molecule of activated and normal states at 0K.

Li and Gainer[95] and Navari *et al.*[87] considered how the addition of polymer to the solvent would alter the terms in the Eyring equation. It may be seen that

$$D/D_0=(\lambda'/\lambda)^2(V_f/V_f')^{1/3}\exp(\varepsilon-\varepsilon'/kT)$$

where the prime indicates properties of the polymer–solvent mix. To evaluate these properties it was boldly assumed that formulae given by Glasstone *et al.*[89] could be applied to dilute polymer solutions. To this end a molecular weight M' (the mass fraction average of solvent and polymer molecular weights) and a molar volume V' (the volume of M' grams of solution) were assigned to the polymer solution; λ' was then replaced by $(V'/N)^{1/3}$, where N is Avogadros number. It is manifest that for high polymers λ' thus calculated will greatly exceed λ, contrary to reasonable expectations. Problems such as this were obscured in the original papers by combination of the λ term with similarly suspect calculations of V_f/V_f'. Finally, agreement with experiment was obtained by proposing an empirical correlation for the exponential term, connecting it with solution viscosity functions. Thus while the theory appears to be moderately successful[96], it has the character of an empirical correlation rather than providing any theoretical insight.

The rate theory approach remains, therefore, useful only in a qualitative way. Experimental determinations of E certainly do provide qualitative insight, and, according to the theory, $E=N\varepsilon'-RT/2$ where ε' may be identified with the sums of energy required to form a hole in the liquid and that needed by the molecule to jump therein.

The free volume approach. Crudely defined, the free volume of a liquid is the difference between its actual volume and the minimum volume which it would occupy if the molecules were packed firmly in contact with each other. Cohen and Turnbull[90] considered diffusion of a trace impurity in a liquid to occur by movement of molecules into voids formed by redistribution of the free volume within the liquid. The voids may be pictured as formed by a general recession of the many surrounding molecules, and filled in by the reverse process[97]. No energy change is associated with the free volume redistribution, but the rate of diffusion is governed by the probability of formation of sufficiently large voids for the molecules to enter. This is shown to be proportional to $\exp(-\gamma V^*/V_f)$ where γ is a numerical factor whose value is between $\frac{1}{2}$ and 1, and V^* is the critical void volume[90]; whence $D_0 \propto \exp(-\gamma V^*/V_f)$. Since usually $V_f \propto T$ at constant pressure, this has the Arrhenius form. However, the theory predicts an entirely different temperature dependence to that of the Eyring equation if D is measured at constant volume rather than constant pressure.

In a binary solution, it is generally assumed that the free volume is equally available to the components. V_f (the average free volume per molecule) is thus redefined as the specific free volume of the mixture $\hat{V}_f$ divided by the number of jumping units per gram, be they molecules or short sections of polymer chains. V_f will thus change with composition for two reasons: firstly, $\hat{V}_f$ will depend on composition according to

$$\hat{V}_f = W_1\hat{V}_f(1) + W_2\hat{V}_f(2) + \Delta\hat{V}_M$$

where W_1, W_2 are weight fractions, $\hat{V}_f(1)$, $\hat{V}_f(2)$ are specific free volumes of the components and $\Delta\hat{V}_M$ is the specific volume change of mixing; secondly, the number of jumping units per gram of mixture $\mathcal{N}$ will depend on composition according to

$$\mathcal{N} = W_1\mathcal{N}(1) + W_2\mathcal{N}(2) = W_1N/M_1 + W_2Nn/M_2$$

where M_1, M_2 are the molecular weights of the components, and component 2 is a polymer with n jumping units per molecule. Since V^* is approximately the volume of the diffusing molecule, it should be independent of composition, whence

$$D/D_0 = \exp[-\gamma V^*(\mathcal{N}/\hat{V}_f - \mathcal{N}(1)/\hat{V}_f(1))]$$

More usually the free volume theory has been used in the study of deviations of D from the diffusion coefficient of the solute in the pure polymer D_P when a low concentration of a plasticizing solvent is present, so that the more usual equation would be

$$D/D_P = \exp[-\gamma V^*(\mathcal{N}/\hat{V}_f - \mathcal{N}(2)/\hat{V}_f(2))]$$

The equation in this form was developed by Vrentas and Duda[97]. However, they also showed that if certain conditions hold, the earlier form due to Fujita[98] may be obtained. These conditions are that $\mathcal{N}(1) = \mathcal{N}(2)$ (i.e. the molecular weight of the polymer jumping unit is equal to that of the solvent), and that $\hat{V}/\hat{V}(2) \simeq 1$ (i.e. the specific volumes of the polymer and of the mixture are very close), from which it follows that

$$D/D_P = \exp\left[-B\left(\frac{1}{f} - \frac{1}{f(2)}\right)\right]$$

where $B = \gamma V^*\mathcal{N}/\hat{V}$ is independent of composition and f, $f(2)$ are the fractional free volumes $\frac{\hat{V}_f}{\hat{V}}$, $\frac{\hat{V}_f(2)}{\hat{V}(2)}$ of the mixture, polymer respectively. If, furthermore, there is no volume change on mixing, we can write $f = f(2) + \beta(1-\varphi)$, where $\beta = f(1) - f(2)$, whence

$$1/\ln(D/D_P) = [f(2) + f^2(2)/\beta(1-\varphi)]/B$$

The theory in the form due to Fujita thus predicts a linear plot of $1/\ln(D_P/D)$ against $1/(1-\varphi)$. B is usually assigned the value of one when no independent insight is available[99-101]; two of the variables D_P, $f(2)$ and β are used to fit the data, although D_P is amenable to direct experiment and independent estimates of $f(2)$ and β are possible from, for example, viscosity and glass transition measurements[98,101,102].

The Fujita version of the free volume theory has been successful for many polymer–organic diluent systems for φ in the range from 1.0 to 0.8. For solvents of small molecular size, however, such as water, the concentration dependence of D is far weaker than might be expected from the theory. This may be due to the assumption of equality of the molecular weight of diffusing solute and polymer jump unit built into the theory[97], although a recent experimental study has supported the idea that the size of the polymer jump unit is related to the size of the other species, and therefore that V_f is of less significance than f, the fractional free volume[101]. The approximation $\hat{V}/\hat{V}(2) \simeq 1$ is certainly reasonable in some region of φ near to unity, but unless $\hat{V}(1) = \hat{V}(2)$ it cannot be valid over a large range of φ. Together with the restriction to systems with no volume change on mixing (i.e. with f a linear function of composition) this will restrict the validity of the expression to large φ[102]. A more serious restriction, however, concerns the applicability of the free volume theory itself. The fractional free volume of the solvent is generally much greater than that of the polymer[102] and, as mentioned above, diffusion in the pure polymer is free volume limited so that, at large φ, increases in solvent concentration will be effective in increasing the rate of diffusion. However, in most solvents, attractive forces are significant as well as free volume. Thus, before applying the free volume theory over the full range of φ, it is important to check that free volume is indeed the rate limiting factor for diffusion in the solvent[103]. For organic solvents at moderate temperatures, free volume effects are expected to be important if not dominant, but for water attractive forces probably predominate[91]; nevertheless, the free volume theory has been applied to aqueous gels of fairly high water content (up to $\varphi = 0.1$)[104]. Some authorities have taken the point of view that the diffusion of small molecules in a polymer–solvent system depends on the ease of a cooperative movement of several polymer segments, which is in turn determined by the available free volume[105], rather than the direct relationship between diffusion and free volume utilized above. According to this picture, a rather abrupt change in the curve of D/D_0 against φ may be anticipated in the region of small φ, corresponding to the transition from solvent with isolated non-overlapping polymer molecules to a uniform pervasion of the whole volume by the polymer segments[100].

According to the free volume theory $D \propto \exp^{-B}/_{f}$ from which it follows that $E = RT^2\partial\ln D/\partial T = (BRT^2\partial f/\partial T)/f^2$; f^2 can be round as detailed above. While it might be expected that all of the increase in volume due to thermal expansion is an increase in free volume, in practice it has been found necessary to make a distinction between free volume available for diffusion and 'interstitial free volume' so that $\partial f/\partial T$ for pure substances cannot be deduced simply from the coefficient of thermal expansion but must be deduced from the dependence of viscosity on temperature[97]. For the binary mixture a reasonable estimate of $\partial f/\partial T$ as being the volume-fraction average of $\partial f(1)/\partial T$ and $\partial f(2)/\partial T$ can be made[99].

RESULTS REVIEW AND DISCUSSION

(1) *Dependence of* D/D_0 *on* φ *and solute size and nature*

Some representative data from the literature are given in *Figures* 3–5 and *Table* 1. The continuous lines in the figures were constructed by visual averaging and interpolation, but are not extrapolated. Where the results were given in the original papers as functions of polymer weight fraction they have been converted to functions of φ using the approximate specific volumes of 0.9, 0.8, 0.8 and 0.6 $cm^3\ g^{-1}$ for polyacrylamide[12], polyvinylpyrrollidone[106], gelatin, and polysaccharide[62] respectively.

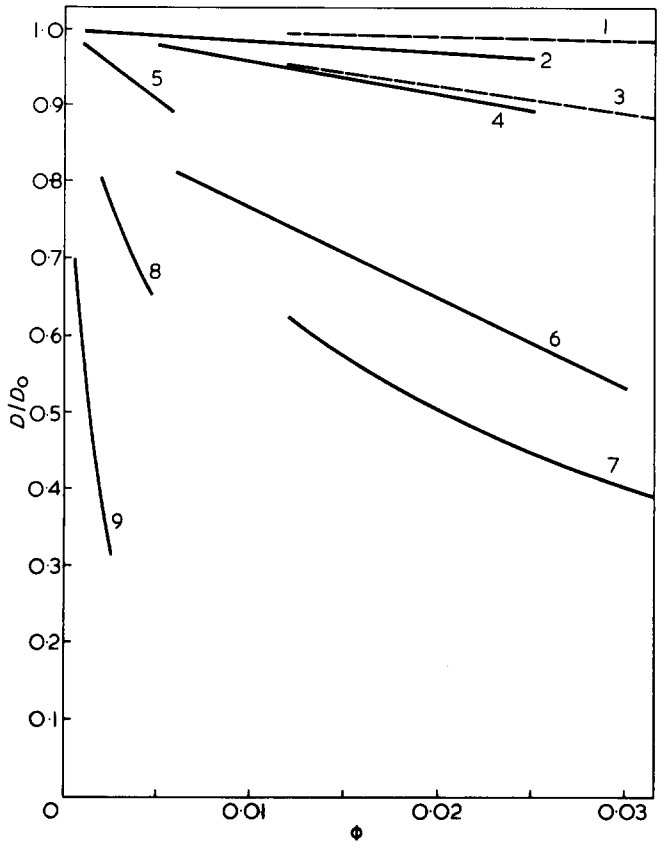

Figure 3 Dependence of relative diffusion rate D/D_0 on polymer volume fraction ϕ

Plot no.	Diffusing species	Solvent	Polymer	Reference
1	Theoretical plot:	D/D_0 =	$1 - \phi/2$	
2	Glycolamide	Water	Various (solutions)	Biancheria and Kegeles[107]
3	Theoretical plot:	$D/D_0 = [(1-\phi)/(1+\phi)]^2$		
4	Cl^-	Water	Agar (gel)	Langdon and Thomas[32]
5	HTO	Water	Agar (gel)	Nakayama and Jackson[108]
6	Urea	Water	Agar (gel)	Friedman[109]
7	Glucose	Water	Hydroxyethyl-cellulose (gel)	Brown *et al.*[80]
8	Bovine serum albumin	Water	Hyaluronic acid (solution)	Laurent *et al.*[110]
9	Turnip mosaic virus	Water	Hyaluronic acid (solution)	Laurent *et al.*[110]

Validity and reproducibility of results. Before attempting to interpret the results, it is desirable to consider their validity. As noted above, White and Dorion[57], Friedman and Kraemer[7], Friedman[109] and Klemm and Friedman[114] all tacitly assumed $K = 1$ so that D will be progressively underestimated as Φ increases. Unfortunately, in the absence of raw data the correct D cannot be determined. The results of Brown, Chitumbo *et al.*[56,80,118] were obtained by a similar experimental method, but K was determined, and the data analysis appears satisfactory (except for the tightly crosslinked cellulose gel which was non-uniform and a somewhat artificial correction was applied to the diffusion coefficients[56]), although their results are exceptionally low (see *Table* 1). The method of Nishijima and Oster[113] may suffer from coupled sucrose and PVP diffusion, since

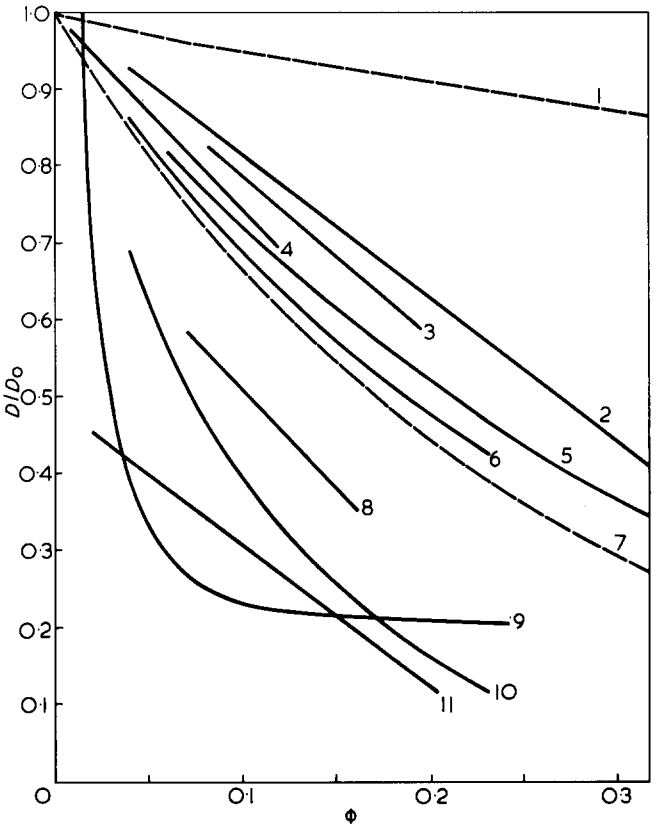

Figure 4 Dependence of relative diffusion rate D/D_0 on polymer volume fraction ϕ

Plot no.	Diffusing species	Solvent	Polymer	Reference
1	Theoretical plot:	D/D_0 =	$1/(1+\phi/2)$	
2	KBr	Water	Gelatin (gel)	Stonham and Kragh[111]
3	H_2O^{18}	Water	Ovalbumin (solution)	Wang[27]
4	Spin-labelled H_2O	Water	Agarose (gel)	Derbyshire and Duff[84]
5	Spin-labelled H_2O	Water	Starch (gel)	Basler and Lechert[112]
6	Urea	Water	Polyacrylamide (gel)	White and Dorion[57]
7	Theoretical plot:	$D/D_0 = [(1-\phi)/(1+\phi)]^2$		
8	Glycerol	Water	Polyacrylamide (gel)	Brown and Johnson[34]
9	Sucrose	Water	PVP, medium molecular weight (solution)	Nishijima and Oster[113]
10	Sucrose	Water	Polyacrylamide (gel)	White and Dorion[57]
11*	Methanol	Benzyl-alcohol	Cellulose acetate (gel)	Klemm and Friedman[114]

* Plotted as polymer weight fraction

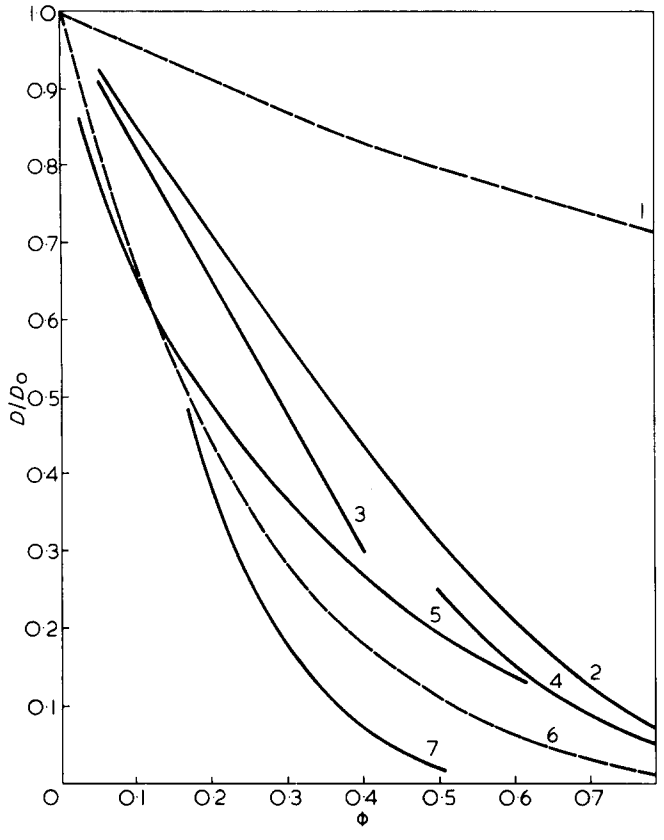

Figure 5 Dependence of relative diffusion rate D/D_0 on polymer volume fraction ϕ

Plot no.	Diffusing species	Solvent	Polymer	Reference
1	Theoretical plot:	$D/D_0 =$	$1/(1+\phi/2)$	
2	C^{14} labelled benzene	Benzene	Rubber	Pattle *et al.*[42]
3	HTO	Water	Various bulky organic electrolytes (solution)	Pikal and Boyd[115]
4	HTO	Water	Various (polymer membranes)	Yasuada *et al.*[104]
5	Spin labelled benzene	Benzene	Polyisobutylene	Boss *et al.*[100]
6	Theoretical plot:	$D/D_0 = [(1-\phi)/(1+\phi)]^2$		
7	C^{14} labelled fructose	Diethylene glycol	Poly hydroxymethyl methacrylate (gel)	Wong *et al.*[116]

the sucrose concentration gradient was rather large: such a problem was observed in the system glycolamide–PVP–water[107].

It should be noted that the values for the self diffusion of water (D_0*) in the literature are fairly scattered[122]—for example, for experiments using HTO as the tracer the values of different workers have ranged from 2.2 to 2.6×10^{-5} cm^2 s^{-1}—a much greater range than the scatter of results found by each individual worker. For this reason D_0* in *Table* 1 has been taken as the value determined in each reference, or otherwise as 2.3×10^{-5} cm^2 s^{-1}. Similar comments apply to the results displayed in *Figures* 3–5. Clearly, uncertainty about the value of D_0 makes it hard to check the data for linearity or extrapolation to D_0 as $\varphi\rightarrow0$.

Some workers have found large differences in D as determined in different preparations of the gel; in particular, Friedman *et al.* reported discrepancies in D of up to 100% for gelatin, agar and cellulose acetate gels[7,109,114] which they attributed to varying structure of the different preparations. However, Stonham and Kragh[111] have reported no significant effect of the viscosity grade on the rate of diffusion of KBr in different gelatin gels. Other workers have reported little effect arising from the degree of crosslinking of gels on the rate of diffusion of small solutes such as used by Friedman *et al.*[57,118]. It is also relevant to note that sucrose and dextran have an equal effect on the conductivity of NaCl solutions[123]; nor does gelation alter the conductivity of gelatin solutions, although a fall in the conductivity of starch slurries has been observed on gelation[124].

It thus appears that the reproducibility problem of Friedman *et al.* is caused by something other than variability in gel structure. For large diffusing molecules, however, the effect of crosslinking is significant[118], and methylene blue diffusion is affected by the grade of gelatin[58].

Obstruction. It is clear that in every case D/D_0 falls below that predicted by the simple obstruction effect for spheres, $D/D_0 = 1/(1+\varphi/2)$. Within the framework of this

Table 1 D/D_0 for labelled water in aqueous gels

Gel	ϕ	D/D_0	References
Calcium alginate (solvent was 60% sucrose solution)	0.01	approx. 0.9	Muhr[117]
Hydroxyethyl-cellulose	0.03	0.24	Brown & Chitumbo[118]
Tobacco mosaic virus (solution)	0.05	0.96	Douglas, Frisch and Anderson[119]
Sodium carboxymethyl cellulose	0.05	0.82	Higdon and Robinson[120]
Agar	0.05	0.87	Woessner,Snowden & Chiu[121]
Polyacrylamide	0.06	0.13	Brown & Chitumbo[118]
Gelatin (solution)	0.08	0.80	Woessner, Snowden & Chiu[121]
Spursely crosslinked cellulose	0.11	0.18	Brown & Chitumbo[118]
Densely crosslinked cellulose	0.11	0.17	Brown & Chitumbo[118]
Dextran	0.12	0.67	Horowitz and Fenichel[2]
Weakly crosslinked polystyrene sulphonate ion exchanger	0.16 (weight fraction)	0.49	Pikal and Boyd[115]
Cellophane film	0.56	0.10	Thau et al.[46] (recalculated by Meares[65])

(For larger values of ϕ further results are given by Meares[65])

theory three possibilities exist for explaining the discrepancy: the obstacles have a more obstructive shape than spheres, the size of the obstacles is enlarged by an impenetrable solvation sheath, and the size of the obstacles is enlarged by an excluded volume effect.

Treatment of the obstacles as needles (the most reasonable spheroid approximation for polymer chains or fibres) still predicts an inadequate reduction in D/D_0, so that they must be treated as oblate spheroids to bring theory and experiment into line according to the first possibility. Woessner and Snowden[125] considered the existence of widely spaced barriers in agar gels as a possible explanation of the smaller reduction of D^*/D_0 found by n.m.r. than by the conventional experiment of Nakayama and Jackson[108]. However, the latter results are also in conflict with conventional experiments for ion diffusion in agar gels[1,3,4,32]. In the absence of any other evidence for the existence of two dimensional impenetrable structures in gels, this possibility is unattractive.

The second possibility has received much attention, and is the basis for Wang's method of finding the hydration of proteins[27]. To calculate the degree of hydration, the volume fraction of polymer obtained by fitting the diffusion data to Fricke's formula (for example) compared to the known volume fraction of unsolvated polymer. In this manner, Langdon and Thomas[32] (curve 4, *Figure 3*) have arrived at the rather high hydration figures of 3.4g H_2O/g anhydrous agar. Wang[27] introduced a further modification and postulated that bound water would further reduce water intra diffusion by the factor $\left(1-\frac{C_{bound}}{C_{total}}\right)$; the results of Derbyshire and Duff[84] and Woessner and Snowden[125] are thus compatible with a much smaller degree of hydration of agar (~0.7g H_2O/g agar). Such values appear reasonable in the light of other techniques for determining bound water. The conductivity data of NaCl in aqueous PEG and PVP solutions[106] and sucrose and dextran solutions[123] may also be interpreted in this way. However, this interpretation would predict unreasonably high degrees of solvation for some of the data—such as all those significantly below curve 3 of *Figure 3* or curve 7 of *Figure 4*.

For very large diffusing molecules, the low values of D/D_0 may be accounted for in terms of a large excluded volume effect—e.g. curves 8, 9 of *Figure* 3. For sufficiently low values of φ, we may replace φ in Fricke's formula for needles by $\Phi=\varphi\frac{(r+\rho)^2}{\rho^2}$. For larger values of φ this formulation breaks down (due to overlap of excluded volumes) and the only approach available is the Ogston equation for D/D_0. Taking the values for the radii r or BSA and TMV as 3.55 nm and 14 nm respectively, and $\rho=0.5$ nm for hyaluronic acid fibres[62], both equations agree sufficiently with the results shown in curves 8, 9 of *Figure* 3 to give credence to the basic idea. However, quantitative agreement is lacking. In this context the inaccuracy of the Ogston equation is disappointing, although it does fit well with the data of Preston and Snowden[62]. Schantz and Lauffer[1] found that Fricke's formula with φ replaced by empirical values of Φ successfully predicted D/D_0 for a variety of solutes, including some proteins (e.g. BSA, $\Phi=0.25$) in 1.5% agar gels. Other workers[9] have also found moderate reduction in the diffusion rate for proteins in agar gels; however, the addition of CMC to an agar gel caused a further drastic decrease in D, probably because of the more homogeneous nature of this system[8] and hence a larger excluded volume effect.

The excluded volume effect may also play a significant role in depressing D/D_0 for moderate size solutes, e.g. curves 6, 7 of *Figure* 3 and curves 8, 9, 10 and 11 of *Figure* 4. For these data, $r\sim\rho$ so that use of Fricke's formula for needles entails replacement of φ by $\Phi\sim4\varphi$. This is still quite inadequate to explain the low values of D/D_0. As noted before, reasonable values for ρ are obtained when fitting the Ogston expression for Φ to partition coefficient data, even for smaller solutes such as glucose and sucrose. Thus the partition coefficient data for sucrose/polyacrylamide of White and Dorion[57] are in tolerable agreement with the Ogston expression for Φ with $r=0.51$ nm and $\rho=0.9$ nm. Use of these values in the Ogston expression for D/D_0 compares well with the data of White and Dorion for diffusion of sucrose in polyacrylamide gels (curve 10, *Figure* 4) at low $\varphi(\varphi<0.05)$, but progressively overestimates D/D_0 for larger φ. Also, even at low φ, the expression overestimates D/D_0 for the diffusion of glucose in a hydroxyethyl cellulose gel (curve 7, *Figure* 3). It is thus clear that the excluded volume effect cannot fully explain these low values found for D/D_0.

Friction and other interactions. Since the low values of D/D_0 found for many systems of moderately sized solutes cannot be explained by the obstruction theory, it seems necessary to postulate an enhanced friction drag on the diffusing molecules doe to the polymer. Support for the existence of significant frictional drag comes from rotational diffusion experiments. Thus for an aqueous hydroxyethyl cellulose gel ($\varphi=0.037$), fluorescein depolarization measurements showed up almost a doubling of friction due to the presence of the polymer[80].

From a knowledge of the fibre radius ρ the rms radius of spherical spaces in the network may be determined[62] as $\rho(\varphi^{-\frac{1}{2}}-1)$. A very crude estimate of the hydrodynamic drag factor may then be made by substitution of this value for R in Faxen's equation. For heterogeneous gels (e.g. agar, where $\rho\sim25$ nm)[55], the hydrodynamic drag thus calculated would be negligible for all but very large solutes. However, for gels in which the polymer chains are unassociated (e.g. polyacrylamide, ~0.9 nm)[62] the predicted additional reduction in D/D_0 is surprisingly close to that found experimentally—e.g. the data of White and Dorion[57] (curve 10, *Figure* 4). Thus while quantitative agreement cannot be hoped for, the hydrodynamic drag effect is probably significant for gels in which the polymer is finely dispersed or for very large solutes in coarse gels.

Both the Ogston theory and the hydrodynamic drag effect (for rigid networks unperturbed by the solute) predict a rapid decline in D/D_0 with increase in solute size. In agreement with the Ogston theory, D/D_0 has been found to be an exponentially decreasing function of r for the diffusion of proteins in dilute hyaluronic acid solutions[62] and for the diffusion of a variety of solutes (ranging from urea to proteins) diffusing in gel membranes[126]. However, for polyacrylamide, hydroxyethylcellulose and cellulose gels, D/D_0 has been found to be virtually independent of solute size for alcohols and oligosaccharides, except for large polyethylene oxide polymers (PEG 3000 and PEG 4000)[118]. More recently similar results have been found

for polyacrylamide gels[34]. Together with the failure of the obstruction theories to account for these results, the independence of D/D_0 on solute size seems to point to an increased 'local viscosity' of the medium[118] (as pointed out recently the notion of 'micro viscosity' of polymer–solvent systems has no definite meaning if solute diffusion depends on solute size or character[127]). It remains unresolved as to whether this could be due to some sort of solute size independent frictional interaction with the polymer, or solvent structuring. It is unfortunate that the effect of solute chemical type has not been studied systematically—although for the polyacrylamide gel D/D_0 has been found to be significantly different for HTO, salts and oligosaccharides[118]. It is interesting also that D/D_0 for glucose diffusion in the hydroxyethylcellulose gel is the same for three different solvents—water, DMSO and DMF. Such results, it seems, point towards the importance of solute–polymer interactions and the dependence of D/D_0 on the particular solute–polymer pair, although it is difficult to see how these interactions would be so important at the low polymer concentrations ($\varphi < 0.05$). As a final work of caution, it should be noted that the results of Brown, Chitumbo *et al.*[80,118] on which much of the above discussion is based, are, for all systems studied, of similar low magnitude. The argument of the significance of solute–polymer interaction is thus considerably weakened when it is observed that HTO diffusion is much more rapid in a covalently crosslinked dextran gel[2] than in the chemically similar cellulose gels of Brown *et al.*[118], while Brown *et al.* find similar rates of diffusion for HTO in the chemically dissimilar gels of cellulose and polyacrylamide (see *Table 1*).

Finally it must be said that factors other than solute size and solvent viscosity play an important role in determining the rate of diffusion in monomeric liquids. Thus, in hydrogen bonding solvents, diffusion of strong hydrogen bonding solutes is selectively reduced[2]. Again, in the system sucrose–water, it has been found that D/D_0 for H_2O[18] agrees well with η_0/η while D/D_0 for labelled sucrose falls more slowly than η/η_0 as the sucrose concentration is increased[41].

Free volume. The free volume theory, in the form due to Fujita, predicts the relationship $D = D_P \exp[1/(p + q/(1-\varphi))]$ (or applying the same derivation from D_0, $D = D_0 \exp[1/(P' + q'/(1-\varphi))]$) where p and q are independent of φ. Such equations have been found to satisfactorily express the variation of D with composition for many systems, for example curves 2, 5 and 7 of *Figure 5*. However, since even $1/\ln\left(\frac{1-\varphi}{1+\varphi}\right)^2$ gives a reasonably linear plot against $1/\varphi$, the theoretical implications of a fit with a Fujita type polt are not great. It is unfortunate that $f(1)$, $f(2)$ and even D_P[92,100,101] have often been regarded as adjustable parameters; few critical studies in which D_P is directly measured and $f(1)$, $f(2)$ determined independently (e.g. from viscosity or glass transition temperature data) have been undertaken, although the values which fit the diffusion data are plausible for organic liquid–polymer systems[99–103,105].

Critical polymer concentration. A number of workers have reported a fairly abrupt fall in the rate of diffusion of probe molecules in polymer solutions as the polymer concentration exceeds a critical value[100,101,113,128]. This has been interpreted as the concentration at which overlap of the polymer molecules commences. While such overlap would certainly have a profound effect on polymer diffusion (since the coupling between segments of a polymer molecule will be affected by the presence of other polymer molecules) it is unclear why it should greatly affect diffusion of small molecules. Furthermore, the results which show this feature are rather exceptional (e.g. curve 9 of *Figure 4*) and the suspicion remains that the feature may be due to interference of the polymer with measurements of solute transport[129].

(2) *Dependence of* D/D_0 *on* T

It is unfortunate that the dependence of D on temperature has not received the attention it deserves in many of the studies of diffusion in polymer solvent systems. However, while it is necessary to obtain accurate diffusivity data to demonstrate the small departure of D/D_0 from unity for the more dilute gels, even more accurate data are required to reveal significant changes in the temperature dependence of D due to the presence of the polymer. For example, Derbyshire and Duff[84] give their results for D the uncertainty of 4%, but their results for E the uncertainty of 13%. Only large differences in E from literature values for E_0 can be taken as significant.

In many gels E has been found to be the same as E_0 within experimental error, pointing to the role of the gel substance as that of inert obstacles. These are: water intradiffusion in starch gels[112] ($0 < \varphi < 0.38$), and agarose gels[84] ($0 < \varphi < 0.13$), diffusion of a variety of solutes in dextran gels[2] ($\varphi = 0.17$), diffusion of glycerol and PEG 600 in a polyacrylamide gel[34] ($\varphi = 0.16$) and diffusion of a number of chlorides in agar gels[130] ($\varphi = 0.003$). However, the activation energy for ionic mobility was found to be considerably greater in a starch gel ($\varphi = 0.26$) than in water[124].

In some systems a progressive increase in E with φ has been found; such results are displayed in *Figure 6*, together with some values of ΔE predicted by the correlation of Navari *et al.*[87] (curves 1, 2 of *Figure 6*). The very rapid increase of ΔE on addition of polymer to the solvent, predicted by the theory of Navari *et al.*, is evidently in sharp contrast to all the experimental results, which display a gradual increase of ΔE with φ at low φ. While no other quantitative prediction of ΔE for polymer solutions has been derived from the rate theory, the qualitative feature of a progressive increse in E with φ for homogeneous systems is in accord with the rate theory. However, there are several alternative qualitative reasons for a change in ΔE—greater energy of solute–polymer bonds than solute–solvent bonds, greater energy to disrupt a 'cage' of polymer molecules due to chain stiffness[92] or the creation of a longer range order in the system due to the polymer[127].

The free volume theory, however, does make the specific prediction of $E = B(RT^2/f^2)\partial f/\partial T$. Once again few workers have checked the validity of this expression, although for cetane intradiffusion in the system cetane–polyisobutylene it has been moderately successful[99].

Brown and Chitumbo[118] have reported sharp discontinuities in the slope of ln D vs. $1/T$ for glucose diffusion in polyacrylamide gels and cellulose gels. The apparent activation energies below 25°C are considerably less than that for free diffusion, while above 25°C they exceed the free diffusion activation energies by an equivalent amount. This exceptional result is interpreted

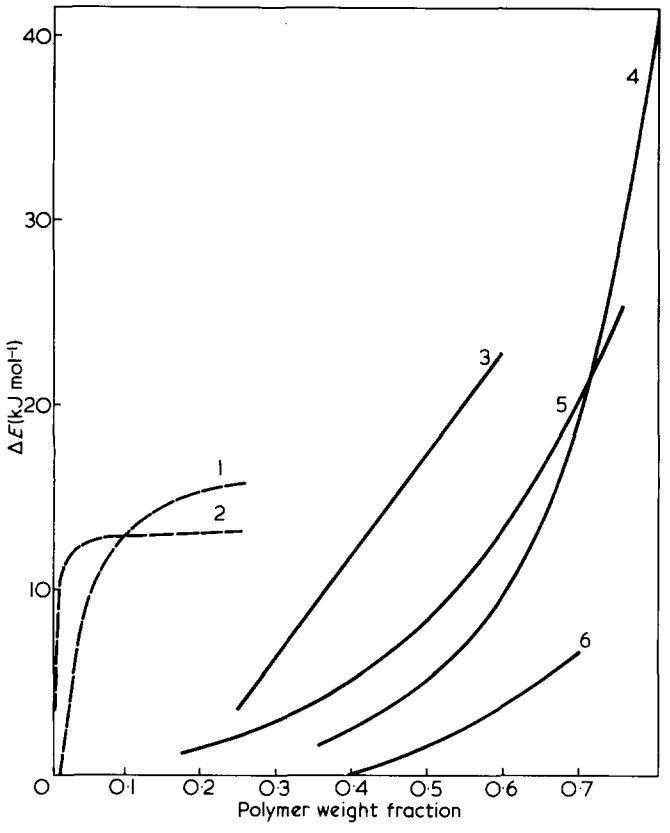

Figure 6 Dependence of excess apparent activation energy ΔE on polymer weight fraction

Plot no.	Diffusing species	Solvent	Polymer	Reference
1	Theoretical plot for any solute	Toluene	Polystyrene	Navari *et al.*[87]
2	Theoretical plot for any solute	Water	CMC	Navari *et al.*[87]
3	KCl	Water	Glycol methacrylate (gels)	Spacek and Kubin[10]
4	Spin-labelled benzene	Benzene	Polystyrene	Kosfeld and Gofloo[92]
5	C^{14} labelled cetane	Cetane	Polyisobutylene	Moore and Ferry[99]
6	Spin-labelled cyclohexane	Cyclohexane	Polystyrene	Kosfeld and Gofloo[92]

as being caused by a sharp increase in mobility of the polymer chains at 25°C. This is analogous to the sharp increase in E found for diffusion of gases and solvents through polymers at their glass transition temperature: when the polymer chains become mobile more energy is required to form 'pores' in between the polymer chains for diffusing molecules, rather than diffusive jumps taking place only between existing 'pores'[131]. While there may be other evidence for a second order transition temperature of 25°C for cellulosic polymers[56,80], the argument is considerably weakened by the occurrence of the same behaviour of diffusion in the polyacrylamide gel at 25°C. Furthermore, no discontinuity of E was observed for glycerol diffusion in a different polyacrylamide gel[34]. Another interesting result is the low value for E found[33] for intradiffusion of chromate ions in an agar gel ($\varphi = 0.006$) containing 0.1M K_2CrO_4.

CONCLUSIONS

Diffusion of micromolecular solutes in the more heterogeneous gels (e.g. agar/water) is only slightly slower than in the solvent and the obstruction theory (e.g. Fricke's equation) is moderately successful in accounting for the effect.

A greater reduction in the diffusion rate of micromolecular solutes seems to occur for the more homogeneous gels (e.g. polyacrylamide/water), although the results in the literature are rather variable. This reduction appears to be the result of a number of factors, including the obstruction effect, hydrodynamic drag and specific solute–polymer interactions. No quantitative assessment of these factors appears possible.

For solvent intradiffusion in organic solvent polymer systems, the free volume theory is valuable in correlating the results. It is not yet clear, however, to what degree the theory is a successful explanation. A similar reduction of the diffusion rate is, for example, predicted by the simplistic stochastic obstruction effect of Mackie and Meares.

Few careful experiments on the diffusion of macromolecules in gels have been reported in the literature. The drastic reduction in the rate of diffusion observed in homogeneous systems is probably due to the limited number of spaces available for the macromolecules in the gel, although distortion of the network may accompany diffusion, in which case a new theoretical approach is required. The more modest reduction of the diffusion rate of macromolecules in gels such as agar demonstrates the coarse structure of these gels.

For a better understanding of diffusion in gels, the following emerge as useful experimental variables: solute size and chemical nature, temperature, gel structure (degree of crosslinking etc.) and solvent nature.

POSTSCRIPT

Subsequent to submission of the paper the authors were informed of another very relevant review, dealing particularly with diffusion of a third component in homogeneous aqueous polymer solutions[132]. As well as presenting new material, some references to experimental work not given above are included. For low molecular weight solutes in dextran solution, an interesting correlation between D/D_0 and K is revealed, but not explained. For compact macromolecular solutes of intermediate size, the theories of Ogston *et al.*[62] and of Langevin and Rondelez[93] have some applicability, while for very large compact macromolecules, $D/D_0 = \eta_0/\eta$. The situation for the transport of long chain polymers in polymer solutions is very complex, and a novel rapid transport phenomenon is described.

ACKNOWLEDGEMENTS

Alan H. Muhr warmly acknowledges financial support from Lyons Central Laboratories and the Agricultural Research Council.

REFERENCES

1 Schantz, E. J. and Lauffer, M. A. *Biochemistry* 1962, **1**, 658
2 Horowitz, S. B. and Fenichel, I. R. *J. Phys. Chem.* 1964, **68**, 3378
3 Slade, A. L., Cremers, A. E. and Thomas, H. C. *J. Phys. Chem.* 1966, **70**, 2840
4 Spalding, G. E. *J. Phys. Chem.* 1968, **73**, 3380
5 Barr, L. W. and Elmessiery, M. A. M. I. *Nature* 1979, **281**, 553
6 Freer, R. and Sherwood, J. N. *J. Chem. Soc. Faraday I* 1980, **76**, 1021
7 Friedman, L. and Kraemer, E. O. *J. Am. Chem. Soc.* 1930, **52**, 1295
8 Wunderly, C. *Clin. Chim. Acta* 1959, **4**, 754
9 Ackers, G. K. and Steere, R. L. *Biochem. Biophys. Acta* 1962, **59**, 137
10 Spacek, P. and Kubin, M. *J. Polym. Sci. C* 1967, **16**, 705
11 Busk, G. C. and Labuza, T. P. *J. Food Sci.* 1979, **44(5)**, 1369
12 Richards, E. G. and Temple, C. J. *Nature (Phys. Sci.)* 1971, **230**, 92
13 Tanaka, T. *Sci. Am.* 1981, **244**, 110
14 Rees, D. A. *Chem. & Ind.* 1972, 630
15 Bryce, T. A., McKinnon, A. A., Morris, E. R., Rees, D. A. and Thorn, D. *Faraday Disc. Chem. Soc.* 1974, **57**, 221
16 Halberstadt, E. S., Henisch, H. K., Nickl, J. and White, E. W. *J. Electrochem. Soc.* 1969, **116**, 1258
17 Tomka, I. and Spuhler, A. 'Symposium on Gelation and Gelling Agents' *Br. Food Manuf. Ind. Res. Assoc., Leatherhead*, 1972, **18**
18 Smidsrød, O. and Skipnes, O. 'Some Physical Properties of Alginates in Solution and in the Gel State' Report no. 34, Norwegian Institute of Seaweed Research, N-7034, Trondheim NTH, Norway, 1973
19 Tal'Roze, R. V., Shibaev, V. P. and Plate, N. A. *J. Polym. Sci. C* 1974, **44**, 35
20 Clark, A. H., Judge, F. J., Richards, J. B., Stubbs, J. M. and Suggett, A. *Int. J. Pept. Protein Res.* 1981, **17**, 380
21 Ogston, A. G. *Trans. Faraday Soc.* 1958, **54**, 1754
22 Ogston, A. G. *J. Phys. Chem.* 1970, **74**, 668
23 Rodbard, D. and Chrambach, A. *Proc. Nat. Acad. Sci. (USA)* 1970, **65**, 970
24 Osmers, H. R. and Metzner, A. B. *Ind. Eng. Chem. Fundam.* 1972, **11**, 161
25 Tyrrell, H. J. V. 'Diffusion and Heat Flow in Liquids', Butterworths, London, 1961, pp 126–128
26 Robinson, R. A. and Stokes, R. H. 'Electrolyte Solutions', 2nd Edition, Butterworths, London, 1959, pp 310–313
27 Wang, J. H. *J. Am. Chem. Soc.* 1954, **76**, 4755
28 Paul, D. R. and Kemp, D. R. *J. Polym. Sci., C* 1973, **41**, 79
29 Paul, D. R. and Koros, W. J. *J. Polym. Sci., A2* 1976, **14**, 675
30 Boyd, G. E. and Soldano, B. A. *J. Am. Chem. Soc.* 1953, **75**, 6091
31 Kurihara, H., Hirakawa, T., Higuchi, H. and Matuura, R. *Bull. Chem. Soc. Jpn.* 1962, **35**, 1740
32 Langdon, A. G. and Thomas, H. C. *J. Phys. Chem.* 1971, **75**, 1821
33 Arnikar, H. J., Patil, S. F., Adhyapak, N. G. and Potdar, J. K. *Z. Phys. Chem. Neue Folge* 1980, **120**, 51
34 Brown, W. and Johnsen, R. M. *Polymer* 1981, **22**, 185
35 Katchalsky, A. and Curran, P. F. 'Nonequilibrium Thermodynamics in Biophysics', Harvard UP, Cambridge, Mass. 1965, 103
36 Crank, J. 'The Mathematics of Diffusion', 2nd Edition, O.U.P., London, 1975, pp 209–214
37 Freise, V. *J. Chim. Phys.* 1957, **54**, 879
38 Guerts, T. J., Walstra, P. and Mulder, H. *Neth. Milk Dairy J.* 1974, **28**, 102
39 Mills, R. *J. Phys. Chem.* 1963, **67**, 600
40 Kirkwood, J. G., Baldwin, R. L., Dunlop, P. J., Gosting, L. J. and Kegeles, G. *J. Chem. Phys.* 1960, **33**, 1505
41 Irani, R. R. and Adamson, A. W. *J. Phys. Chem.* 1958, **62**, 1517
42 Pattle, R. E., Smith, P. J. A. and Hill, R. W. *Trans. Faraday Soc.* 1967, **63**, 2389
43 de Groot, S. R. and Mazur, P. 'Non-equilibrium Thermodynamics', 1st Edition, North Holland, Amsterdam, 1962, pp 239–261
44 Duda, J. L. and Vrentas, J. S. *Ind. Eng. Chem. Fund.* 1965, **4**, 301
45 Devell, L. *Acta Chem. Scand.* 1962, **16**, 2177
46 Thau, G., Bloch, R. and Kedem, O. *Desalination* 1966, **1**, 129
47 Ghai, R. K., Ertl, H. and Dullien, F. A. L. *Am. Inst. Chem. Eng. J.* 1973, **19**, 881
48 Bearman, R. J. *J. Phys. Chem.* 1961, **65**, 1961
49 Paul, D. R. and Ebra-Lima, O. M. *J. Appl. Polym. Sci.* 1975, **19**, 2759
50 Vrentas, J. S. and Duda, J. L. *Am. Inst. Chem. Eng. J.* 1979, **25**, 1
51 Fish, B. P. 'Diffusion and Equilibrium Properties of Water in Starch', Food Investigation Technical Paper no. 5 HMSO, London, 1957, Ch. 6
52 Park, G. S. 'Diffusion in Polymers' (Eds. J. Crank and G. S. Park), Academic Press, London, 1968, Ch. 5
53 Beck, R. E. and Schultz, J. S. *Biochim. Biophys. Acta 1972*, **255**, 273
54 Satterfield, C. N., Colton, C. K. and Pitcher, W. H. *Am. Inst. Chem. Eng. J.* 1973, **19**, 628
55 Laurent, T. C. *Biochim. Biophys. Acta* 1967, **136**, 199
56 Chitumbo, K. M. 'Sorption and Diffusion in Dilute Cellulosic Networks', Uppasala Dissertations from the Faculty of Science, no. 10, Uppsala, 1975, pp 59–61
57 White, M. L. and Dorion, G. H. *J. Polym. Sci.* 1961, **55**, 731
58 Nixon, J. R., Georgakopoulos, P. P. and Carless, J. E. *J. Pharm. Pharmacol.* 1967, **19**, 246
59 Marignan, R. and Crouzat-Reynes, G. *Trav. Soc. Pharm. Montpelier* 1956, **16**, 171
60 Dumanski, A. *Kolloid Z.* 1908, **3**, 210
61 Weibel, E. R. *Lab. Invest.* 1963, **12**, 131
62 Ogston, A. G., Preston, B. N. and Wells, J. D. *Proc. R. Soc. Lond., A* 1973, **333**, 297
63 Higuchi, W. I. and Higuchi, T. *J. Am. Pharm. Assoc. (Sci. Edn.)* 1960, **49**, 598
64 Lauffer, M. A. *Biophys. J.* 1961, **1**, 205
65 Meares, P. *Philos. Trans. R. Soc. London, B* 1977, **278**, 113
66 Carman, P. C. 'Flow of Gases through Porous Media', Butterworths, London, 1956, pp 45–50
67 Mackie, J. S. and Meares, P. *Proc. R. Soc. Lond., A* 1955, **232**, 498
68 Ferguson, H., Gardner, C. R. and Paterson, R. *J. Chem. Soc. Faraday Trans. I*, 1972, **68**, 2021
69 Boyack, J. R. and Giddings, J. C. *Arch. Biophys. Biochem.* 1963, **100**, 16
70 Barrer, R. M. 'Diffusion in Polymers' (Eds. J. Crank and G. S. Park), Academic Press, London, 1968, Ch. 6
71 Crank, J. 'The Mathematics of Diffusion', 2nd Edition, Oxford U.P., 1975, pp 266–285
72 Fricke, H. *Phys. Rev.* 1924, **24**, 575
73 Hashin, Z. and Shtrikman, S. *J. Appl. Phys.* 1962, **33**, 3125
74 Waldmann-Meyer, H. M. 'Chromatography of Synthetic and Biological Polymers', Vol. 1, Ellis Horwood Ltd., Chichester, 1978, Ch. 9
75 Faxen, H. *Ark. Mat. Astron. Fys.* 1923, **17**, no. 27
76 Broersma, S. *J. Chem. Phys.* 1958, **28**, 1158
77 Clough, S. B., Read, H. E., Metzner, A. B. and Behn, V. C. *Am. Inst. Chem. Eng. J.* 1962, **8**, 346
78 Wasan, D. T., Lynch, M. A., Chad, K. J. and Srinivasan, N. *Am. Inst. Chem. Eng. J.* 1972, **18**, 928
79 Biddle, D. *Ark. Kem.* 1968, **29**, 553
80 Brown, W., Kloow, G., Chitumbo, K. and Amu, T. *J. Chem. Soc. Faraday Trans. I*, 1976, **72**, 485
81 Laurent, T. C. and Obrink, B. *Eur. J. Biochem.* 1972, **28**, 94
82 Preston, B. N., Obrink, B. and Laurent, T. C. *Eur. J. Biochem.* 1973, **33**, 401
83 Weber, G. *Adv. Protein Chem.* 1953, **8**, 415
84 Derbyshire, W. and Duff, I. D. *Faraday Discuss. Chem. Soc.* 1974, **57**, 243
85 Metzner, A. B. *Nature* 1965, **208**, 267
86 Quinn, J. A. and Blair, L. M. *Nature* 1967, **214**, 907
87 Navari, R. M., Gainer, J. L. and Hall, K. R. *Am. Inst. Chem. Eng. J.* 1971, **17**, 1028
88 Wang, J. H. *J. Phys. Chem.* 1954, **58**, 686
89 Glasstone, S., Laidler, K. J. and Eyring, H. 'The Theory of Rate Processes', McGraw-Hill Inc., USA, 1941, Ch. 9
90 Cohen, M. H. and Turnbull, D. *J. Chem. Phys.* 1959, **31**, 1164
91 Macedo, P. B. and Litovitz, T. A. *J. Chem. Phys.* 1965, **42**, 245
92 Kosfeld, R. and Gofloo, K. *Koll. Z. und Z. Polym.* 1971, **247**, 801
93 Langevin, D. and Rondelez, F. *Polymer* 1978, **19**, 875
94 Bode, H. J. *Z. Naturforsch* 1979, **34C**, 512
95 Li, S. U. and Gainer, J. L. *Ind. Eng. Chem. Fundam.* 1968, **7**, 433
96 Jones, R. C. and Gainer, J. L. *Ind. Eng. Chem. Fundam.* 1976, **15**, 83
97 Vrentas, J. S. and Duda, J. L. *J. Polym. Sci., A2* 1977, **15**, 403
98 Fujita, H. 'Diffusion in Polymers', (Eds. J. Crank and G. S. Park), Academic Press, London, 1968, pp 98–100
99 Moore, R. S. and Ferry, J. D. *J. Phys. Chem.* 1962, **66**, 2699
100 Boss, B. D., Stejskal, E. D. and Ferry, J. D. *J. Phys. Chem.* 1967, **71**, 1501
101 Ferguson, R. D. and von Meerwall, E. *J. Polym. Sci., A2* 1980, **18**, 1285
102 Machin, D. and Rogers, C. E. *Makromol. Chem.* 1972, **155**, 269

103 Vrentas, J. S. and Duda, J. L. *J. Polym. Sci., A2* 1977, **15**, 417
104 Yasuda, H., Lamaze, C. E. and Peterlin, A. *J. Polym. Sci., A2* 1971, **9**, 1117
105 Kosfeld, R. and Zumkley, L. Ber. *Bunsenges. Phys. Chem.* 1979, **83**, 392
106 Elworthy, P. H., Florence, A. T. and Rahman, A. *J. Phys. Chem.* 1972, **76**, 1763
107 Biancheria, A. and Kegeles, G. *J. Am. Chem. Soc.* 1957, **79**, 5908
108 Nakayama, F. S. and Jackson, R. D. *J. Phys. Chem.* 1963, **67**, 932
109 Friedman, L. *J. Am. Chem. Soc.* 1930, **54**, 1311
110 Laurent, T. C., Bjork, I., Pietruszkiewicz, A. and Persson, H. *Biochim. Biophys. Acta* 1963, **78**, 351
111 Stonham, J. P. and Kragh, A. M. *J. Photogr. Sci.* 1966, **14**, 97
112 Basler, W. and Lechert, H. *Stärke* 1974, **26**, 39
113 Nishijima, Y. and Oster, G. *J. Polym. Sci.* 1956, **19**, 337
114 Klemm, K. and Friedman, L. *J. Am. Chem. Soc.* 1932, **54**, 2637
115 Pikal, M. J. and Boyd, G. E. *J. Phys. Chem.* 1973, **77**, 2918
116 Wong, C. P., Schrag, J. L. and Ferry, J. D. *J. Polym. Sci., A2* 1971, **9**, 1725
117 Muhr, A. H. unpublished results
118 Brown, W. and Chitumbo, K. *J. Chem. Soc. Faraday Trans. 1* 1975, **71**, 12
119 Douglass, D. C., Frisch, H. L. and Anderson, E. W. *Biochim. Biophys. Acta* 1960, **44**, 401
120 Higdon, W. T. and Robinson, J. D. *J. Chem. Phys.* 1962, **37**, 1161
121 Woessner, D. E., Snowden, B. S. and Chiu, Y. C. *J. Coll. Int. Sci.* 1970, **34**, 283
122 Mills, R. *J. Phys. Chem.* 1973, **77**, 685
123 Carpenter, D. O., Hovey, M. M. and Bak, A. F. *Ann. N.Y. Acad. Sci.* 1973, **204**, 502
124 Collison, R. *Nature* 1960, **188**, 1105
125 Woessner, D. E. and Snowden, B. S. *J. Col. Int. Sci.* 1970, **34**, 290
126 Colton, C. K., Smith, K. A., Merrill, E. W. and Farrell, P. C. *J. Biomed. Mater. Res.* 1971, **5**, 459
127 Bagdonaite, V. A., Juskeviciute, S. S. and Shlyapnikov, Yu. A. *Polymer* 1981, **22**, 145
128 Malinski, T. and Zagorski, Z. P. *Polymer* 1979, **20**, 433
129 Nyström, B., Moseley, M. E., Stilbs, P. and Roots, J. *Polymer* 1981, **22**, 218
130 Stiles, W. Proc. R. Soc. 1923, **103A**, 260
131 Manson, J. A. and Chiu, E. H. *J. Polym. Sci., C* 1973, **41**, 95
132 Preston, B. N., Laurent, T. C. and Comper, W. D. to be published in 'Glycosaminoglycan Assemblies in the Extracellular Matrix' (Eds. S. Arnott and D. A. Rees), Humana Press