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Physical models of diffusion for polymer solutions, gels and solids

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Abstract

Diffusion in polymer solutions and gels has been studied by various techniques such as gravimetry, membrane permeation, fluorescence and radioactive labeling. These studies have led to a better knowledge on polymer morphology, transport phenomena, polymer melt and controlled release of drugs from polymer carriers. Various theoretical descriptions of the diffusion processes have been proposed. The theoretical models are based on different physical concepts such as obstruction effects, free volume effects and hydrodynamic interactions. With the availability of pulsed field gradient NMR techniques and other modern experimental methods, the study of diffusion has become much easier and data on diffusion in polymers have become more available. This review article summarizes the different physical models and theories of diffusion and their uses in describing the diffusion in polymer solutions, gels and even solids. Comparisons of the models and theories are made in an attempt to illustrate the applicability of the physical concepts. Examples in the literature are used to illustrate the application and applicability of the models in the treatment of diffusion data in various systems. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Diffusion theories; Diffusion models; Self-diffusion; Diffusant diffusion; Polymers; Gels

Contents

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Nomenclature

α	Parameter dependent on the diffusant size in Phillies' model [52,101,102], and independent of the diffusant size in the model of Altenberger et al. [97]
β	Constant dependent on the solute size and on the temperature in the model of Petit et al. [33]
c	Concentration (g/ml)
c^*	Critical overlap concentration, or overlap concentration, at which the entanglement of polymer chains starts according to Refs. [122,123]
c_e	Entanglement concentration, $c_e \approx c^*$ according to Refs. [137,138]
D	Diffusion coefficient (m^2/s) (self- or tracer diffusion coefficient)
D_0	Diffusion coefficient in the absence of the polymer network (m^2/s)
E_a	Activation energy (kJ/mol)
ΔE	Energy barrier (kJ/mol)
φ_p	Volume fraction of polymer
φ_s	Volume fraction of solvent
HPC	Hydroxypropyl cellulose
HPMC	Hydroxypropyl methyl celluclose
κ	Screening parameter in Cukier's model [26]
k	Jump frequency in the model of Petit et al. [33], which depends on temperature and diffusant size
k_B	Boltzmann's constant (1.380658×10^{-23} J K^{-1})

M	Polymer molecular weight
M_c	Number-average molecular weight between cross-links
M_c^*	Theoretical molecular weight between cross-links below which diffusion of a solute of size r_s could not occur, in the model of Peppas and Reinhart [195]
M_n	Number-average molecular weight of uncross-linked polymer
ν	Scaling parameter characteristic of the system in Phillies' model [52,101,102], and parameter dependent on the system in the model of Petit et al. [33]
NMR	Nuclear magnetic resonance
P	Matrix polymer molecular weight in the model of de Gennes [123]
PA	Polyacrylamide
PEG	Poly(ethylene glycol)
PGSE	Pulsed-gradient spin-echo
PMA	Poly(methyl acrylate)
PMMA	Poly(methyl methacrylate)
PS	Polystyrene
PVA	Poly(vinyl alcohol)
PVAc	Poly(vinyl acetate)
PVME	Poly(vinyl methyl ester)
ρ	Radius of the polymer or fiber (Å)
R_h	Hydrodynamic radius of the diffusing molecule (Å)
R_g	Radius of gyration (Å)
T	Temperature (K)
T_g	Glass transition temperature
THF	Tetrahydrofuran
ξ	Correlation length or network mesh size as defined by de Gennes [123], and end-to end distance of a polymer chain in the model of Amsden [28]

1. Introduction

Diffusion is the process responsible for the movement of matter from one part of a system to another [1], and it is mainly due to random molecular motions. In gases, diffusion processes are fast (10 cm/min) whereas they are much slower in liquids (0.05 cm/min) and solids (0.00001 cm/min) [2]. According to Cussler [2], diffusion in both gases and liquids can be successfully predicted by theories. Diffusion is known to depend on temperature, pressure, solute size and viscosity. Diffusion has a much larger range of values in solids, where diffusion coefficients can differ by more than a factor of 10^{10}. Therefore, diffusion in solids is difficult to estimate with theoretical models [2]. Diffusion in polymers is complex and the diffusion rates should lie between those in liquids and in solids. It depends strongly on the concentration and degree of swelling of polymers. Consequently, it remains a challenge to understand, predict and control the diffusion of small and large molecules in polymer systems. The theories and physical models of diffusion may help to realize these goals.

The first mathematical treatment of diffusion was established by Fick [3] who developed a law for diffusion in one dimension:

$$J = -Aj = -AD\frac{\partial c}{\partial z} \tag{1}$$

where J is the flux, j the flux per unit area, A the area across which diffusion occurs, D the diffusion coefficient, c the concentration, z the distance and $\frac{\partial c}{\partial z}$ the gradient of the concentration along the z axis. This equation is also known as Fick's first law. In the case of diffusion without convection and a unitary area, Eq. (1) can be written as

$$J = -D\frac{\partial c}{\partial z}. \tag{2}$$

Eq. (2) is the starting point of numerous models of diffusion in polymer systems.

In the study of solvent diffusion in polymers, different behaviors have been observed. It is known that the diffusion of the solvent is linked to the physical properties of the polymer network and the interactions between the polymer and the solvent itself. Alfrey et al. [4] proposed a classification according to the solvent diffusion rate and the polymer relaxation rate: Fickian (Case I) and non-Fickian (Case II and anomalous) diffusions. The amount of solvent absorbed per unit area of polymer at time t, M_t, is represented by

$$M_t = kt^n \tag{3}$$

where k is a constant and n a parameter related to the diffusion mechanism, the value of which lies between 1/2 and 1. Eq. (3) can be used to describe solvent diffusional behaviors for any polymer–penetrant system whatever the temperature and the penetrant activity.

1.1. Fickian diffusion

Fickian diffusion (Case I) is often observed in polymer networks when the temperature is well above the glass transition temperature of the polymer (T_g). When the polymer is in the rubbery state, the polymer chains have a higher mobility that allows an easier penetration of the solvent [5]. Therefore, Fickian diffusion is characterized by a solvent diffusion rate, R_{diff}, slower than the polymer relaxation rate, R_{relax} ($R_{\mathrm{diff}} \ll R_{\mathrm{relax}}$). A large gradient of solvent penetration is observed in the system. The solvent concentration profile shows an exponential decrease from the completely swollen region to the core of the polymer. The diffusion distance is proportional to the square-root of time [6]

$$M_t = kt^{1/2}. \tag{4}$$

Few examples of Fickian diffusion in polymer systems are reported in the literature, since solvent absorption studies have been often carried out at ambient temperature which is often below T_g. Nevertheless, Fickian diffusion can be observed in polymer systems below T_g with the addition of a plasticizer. Grinsted et al. [5] studied the diffusion of methanol in poly(methyl methacrylate) (PMMA) as a function of water concentration by NMR imaging. They found that the diffusion rate of methanol increased with increasing water concentration. In addition, the diffusion of methanol changed from Case II (see Section 1.2) to Fickian when the water content was increased. This change in methanol diffusional behavior was explained by the presence of water that acted as a plasticizer. Ercken et al. [7] also reported studies of methanol diffusion in PMMA. They showed that methanol diffusion followed Case II behavior at ambient temperature, whereas Fickian behavior was observed at higher temperatures.

1.2. Non-Fickian diffusion

Non-Fickian diffusion processes are mainly observed in glassy polymers, i.e. when the temperature of study is below T_g. At a specific temperature below T_g, the polymer chains are not sufficiently mobile to permit immediate penetration of the solvent in the polymer core [5]. Two kinds of non-Fickian diffusion were defined: Case II diffusion and anomalous diffusion. The main difference between these two diffusion categories concerns the solvent diffusion rate. In Case II diffusion, the solvent diffusion rate is faster than the polymer relaxation process ($R_{\mathrm{diff}} \gg R_{\mathrm{relax}}$), whereas in anomalous diffusion the solvent diffusion rate and the polymer relaxation are about the same order of magnitude ($R_{\mathrm{diff}} \sim R_{\mathrm{relax}}$) [4].

In general, Case II diffusion is observed when solvents have high activities [8]. The characteristics of Case II diffusion are the following: (1) a rapid increase in the solvent concentration in the swollen region which leads to a sharp solvent penetration front between the swollen region and the inner polymer core; (2) the solvent concentration is quite constant in the swollen region behind the solvent penetration front; (3) the solvent penetration front is sharp and advances at a constant rate, thus the diffusion distance is directly proportional to time

$$M_t = kt. \tag{5}$$

(4) There is an induction time of Fickian concentration profile which precedes the solvent penetration front into the glassy polymer core [9–13].

Fickian and Case II diffusions are considered as limiting types of transport processes. Anomalous diffusion lies in between and is characterized by the following equation:

$$M_t = kt^n \text{ and } \tfrac{1}{2} < n < 1. \tag{6}$$

Examples of Case II diffusion with polymer/solvent systems are abundant in the literature. For example, Weisenberger and Koenig [14] showed that methanol diffusion in PMMA obeys Eq. (5) (Case II). Dioxane in polystyrene (PS) [15], acetone in poly(vinyl chloride) [16] and in polycarbonate [6] have the same diffusional behavior.

1.3. Self-diffusion and mutual diffusion coefficients

According to Fick's first law (Eq. (1)), the diffusion coefficient is defined as the rate of transfer of the diffusant across the diffusion section divided by the space gradient concentration at this specific section. If we consider the mixing of two pure species, A and B, without volume variation, then an equal quantity of each component will be transferred in the opposite direction. From a diffusion point of view, we obtain one diffusion coefficients related to both species, referred to as the *mutual diffusion coefficient* [1,17]. However, it is important to note that the mutual diffusion coefficient, D_{m}, can be expressed as the sum of two *intrinsic diffusion coefficients* related to each individual component [17]:

$$D_{\mathrm{m}} = V_{\mathrm{A}}C_{\mathrm{A}}(D_{\mathrm{B}} - D_{\mathrm{A}}) + D_{\mathrm{A}} \tag{7}$$

where C_{A} is the amount of component A contained in the system, V_{A} the constant volume of component A and D_i the intrinsic diffusion coefficient of component *i*.

In already equilibrated systems such as polymer solutions and gels, there is no volume variation and no mass transfer. Nevertheless, the molecules are in motion and diffusion occurs without the presence of a concentration gradient. In this case the diffusion is defined by the *self-diffusion coefficient*. This

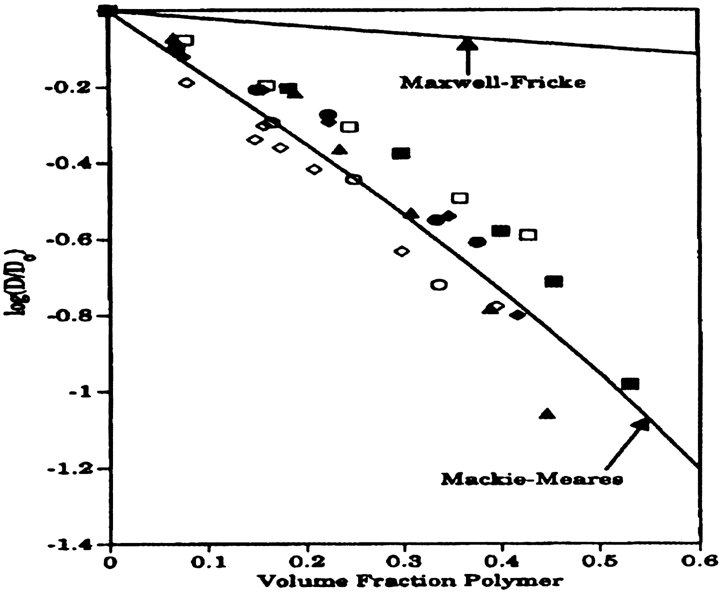

Fig. 1. Semilogarithmic plot of solvent self-diffusion coefficient as a function of the polymer concentration: closed diamonds, toluene–PS; closed triangles, *tert*-butyl acetate–PS; closed circles, ethylbenzene–PS; open circles, cumene–PS; closed squares, chloroform–PS; open triangles, methyl-methacrylate–PMMA; and open squares, methylethylketone. The prediction of the Maxwell–Fricke model (Eq. (9)) and the model of Mackie and Meares (Eq. (10)) are represented by solid lines. Reprinted with permission from Macromolecules 1993;26:6841. ©1999 American Chemical Society [36].

diffusion coefficient can be related to the intrinsic diffusion coefficient (thus indirectly related to the mutual diffusion coefficient) by [17]

$$D_A = DC_A \frac{\partial \mu_A}{\partial C_A} = RTD \frac{\partial \ln a_A}{\partial \ln C_A} \tag{8}$$

where D is the self-diffusion coefficient of component A, μ_A the chemical potential and a_A the thermodynamic activity of component A.

Generally speaking, self-diffusion occurs in systems composed of chemical species in the same phase, such as polymer solutions. When the concentration of the studied species is very small, the self-diffusion of the species is also called *tracer diffusion*. Tracer diffusion also includes the diffusion of chemical species in different physical states, for example, the diffusion of water vapor in a polymer thin film, which involves the diffusion of a gas in a solid [2].

Most diffusion studies have been carried out by measuring the self-diffusion coefficient as it is more convenient to study the already equilibrated systems. In this review article, the applicability of the diffusion models in tracer and self-diffusion will be discussed as described in the literature.

1.4. Diffusion in polymers

Diffusion in polymer solutions and gels have been studied for decades by the use of various techniques such as gravimetry [18], membrane permeation [19], fluorescence [20] and dynamic light scattering

[21]. The studies have resulted in a better knowledge on polymer morphology and structure [22], transport phenomena [23] and, more recently, the controlled release of drugs from polymer carriers [24]. In addition, these studies have led to theoretical descriptions of the diffusion of solvents and/or solutes in polymer solutions, gels and even solids [25–27]. These physical models are based on different physical concepts (the obstruction effects, the hydrodynamic interactions and the free volume theory) and their applicability varies [28]. With the development of modern techniques such as the pulsed-gradient nuclear magnetic resonance (NMR) spectroscopy [29], the study of diffusion has become much easier than with the other techniques mentioned above [30]. With the availability of the diffusion data, several new models of diffusion, concepts, as well as modifications or improvements of the existing theories have appeared in the literature in the last decade [28,31–33]. Limitations in the use of many of these models have been observed in the literature [28,31,34–59]. Review articles have been published by Murh and Blanshard [60], von Meerwall [61,62] and Tirrell [63]. It is the intention of this article to review the various theoretical models, the recent development and the use of the models in the interpretation of the experimental results of diffusion in polymers.

2. Theories and physical models of diffusion

We intend to use homogeneous notations in the text, but the physical significance of the symbols may still differ, which will be indicated.

2.1. Diffusion models based on obstruction effects

In the diffusion models based on obstruction effects, polymer chains are regarded as motionless relative to the diffusing molecules, i.e. solvents and/or solutes. This approximation is based on the assumption that the polymer self-diffusion coefficient is much smaller than that of the diffusant. Thus the polymer is represented as fixed and impenetrable segments immersed in a solution. The presence of the motionless polymer chains leads to an increase in the mean path length of the diffusing molecules between two points in the system.

2.1.1. The Maxwell–Fricke model

The obstruction concept was first introduced by Fricke [25] in 1924 who studied electric conductivity and capacitance of spheroids dispersed in dog blood medium. In this study, the author considered different geometries of spheroids (oblates and prolates) and the best results were obtained with spheres. The following equation was given [36]:

$$\frac{D(1-\varphi)}{D_0} = \frac{1-\varphi'}{1+\varphi'/\chi} \tag{9}$$

where D is the diffusion coefficient, D_0 is the diffusion coefficient in pure solvent, φ is the volume fraction of the polymer, φ' is the volume fraction of the polymer plus non-diffusing solvent bound to the polymer, and χ is a factor depending on the solvent shape (ranging from 1.5 for rods to 2.0 for spheres). This model was called the Maxwell model [64,65] or the Maxwell–Fricke model [36,37].

Langdon and Thomas [66] studied mutual diffusion coefficient of small diffusants such as anions ($^{36}Cl^-$, $^{131}I^-$) and a cation ($^{22}Na^+$) in agar gels of composition ranging from 0.67 to 4 wt%, by

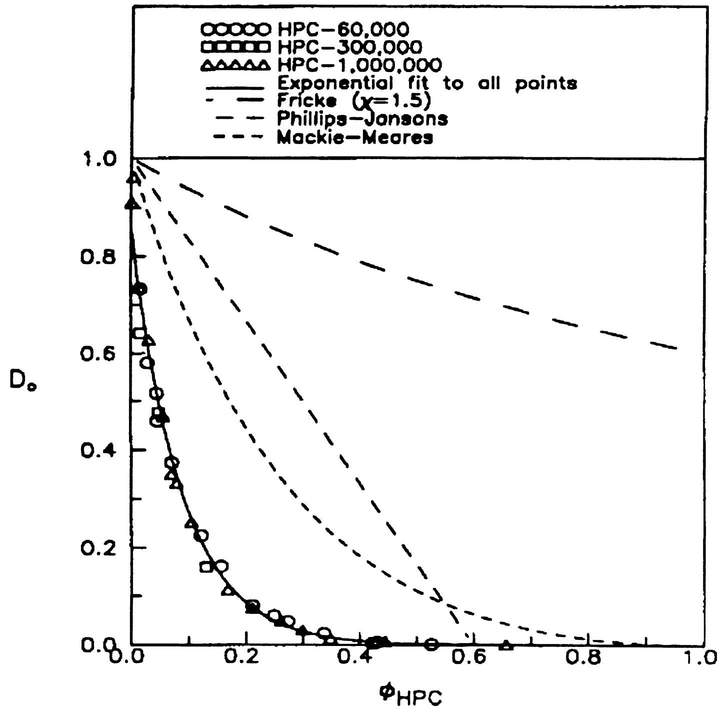

Fig. 2. Normalized self-diffusion coefficient of fluorescein dye as a function of the polymer volume fraction. Reprinted with permission from Macromolecules 1993;26:370. ©1999 American Chemical Society [35].

radioactive labeling (soft β-emitters). They found a linear dependence of the self-diffusion coefficient on the gel composition, when the electrolyte concentration was below 0.1 M. Their analysis in regard to the Maxwell–Fricke model suggested that the hindrance to diffusion was due to the hydration of the agar molecules. According to Cheever et al. [64], diffusion of water in a suspension of latex at low concentrations was predicted correctly by the Maxwell–Fricke model. Griffith et al. [37] reported that the diffusion of water in a suspension of impenetrable spherical particles which showed no hydration effect was closely predicted by this model. Therefore, the Maxwell–Fricke model seems to provide good results for small diffusing particles in dilute polymer solutions. Waggoner et al. [36] showed that this model overestimates the diffusion coefficient at higher polymer concentrations. They studied the self-diffusion of solvents (toluene, ethylbenzene, cumene, *tert*-butyl acetate, chloroform and methylethylketone) in PS and PMMA systems. The polymer concentration ranged from 0 up to 50 wt%. From their data, it is clear that the Maxwell–Fricke model did not fit well the experimental data even for low polymer concentrations, as shown in Fig. 1. The same results were observed by Mustafa et al. [35], who studied the self-diffusion coefficient of fluorescein dye in dilute and concentrated aqueous hydroxypropyl cellulose gels (φ_{HPC} ranging from 0 to 0.65) as illustrated in Fig. 2.

The Maxwell–Fricke equation gives a dependence of the self-diffusion coefficient on the polymer volume fraction and on the solvent shape, φ and χ, respectively. However, the diffusion is closely linked to the size of the diffusant. For example, variation of the self-diffusion coefficient between a small molecule such as water ($D = 2.77 \times 10^{-9}$ m^2/s) and a macromolecule such as poly(ethylene glycol) with a molecular weight of 2000 ($D = 1.73 \times 10^{-10}$ m^2/s) in the same poly(vinyl alcohol) (PVA) system ([PVA] = 0.03 g/ml, $T = 43$°C) is more than one order of magnitude and far from being identical [67].

Therefore, this model can be used in the study of small molecules such as solvents [36] in dilute polymer solutions [37] and/or gas diffusion in highly swollen membranes, for which the difference of self-diffusion coefficients is insignificant for the different diffusants.

2.1.2. The model of Mackie and Meares

In 1955, Mackie and Meares [68] employed the physical concept proposed by Fricke to describe the diffusion of electrolytes in a resin membrane, assuming that the polymer mobility is less important than the mobility of ions or water, so that sites occupied by the polymer are permanently unavailable to ions or water. Thus, the motionless polymer chains impose a tortuosity or an increase in the path length for the molecules in motion. The diffusion coefficient of a small molecule, equal in size to the monomer segment in the polymer, is given by the following equation:

$$\frac{D}{D_0} = \left[\frac{1-\varphi}{1+\varphi}\right]^2 \tag{10}$$

where D, D_0 and φ are the same as defined for Eq. (9).

This model provided satisfactory results over a wide range of concentrations (up to 60 wt% of cellulose) as shown by Brown and coworkers [69–71]. Their work was based upon a series of diffusants with increasing size: water, *tert*-butanol, dioxane, [69] ethylene glycol, poly(ethylene glycol), oligosaccharides and poly(hydric alcohol) [70]. In each case, they analyzed the data in regard to the model of Mackie and Meares. These studies led to the conclusion that the diffusion of small-sized diffusants can be described by the obstruction model, while for oligomers and polymers they observed a weaker correlation between the experimental data and the theory. The authors attributed this divergence to the interactions between the larger diffusants and the polymer chains. In a later work, Brown et al. [71] studied the diffusion of diffusants with increasing size such as ethylene glycol and 15-crown-5 in cellulose gels. The results were analyzed with the model of Mackie and Meares and another model defined by Wang [72]:

$$\frac{D}{D_0} = 1 - \alpha\varphi \tag{11}$$

where α is a parameter depending on the diffusant geometry (1.5 for prolate and 3 for oblate ellipsoids). This model is also based on the obstruction effect and is generally used to describe diffusion in microemulsion systems [35,73]. Despite the introduction of a diffusant shape parameter, comparison between these two models led to the conclusion that Wang's model was valid only for small diffusants in the dilute regime, whereas the model of Mackie and Meares was valid for regimes slightly more concentrated [71]. However, their results showed that neither model is in good agreement with the data in the concentrated regions. The divergence is smaller with the model of Mackie and Meares in semi-dilute regime but keeps on increasing with higher polymer concentration [71].

The model of Mackie and Meares has provided satisfactory results for the diffusion of molecules of various sizes in cellulose networks with polymer concentration up to 60 wt% as well as for the diffusion of organic solvents in PS and PMMA, as shown in Fig. 1. However, this model showed significant deviations from the experimental data with large diffusants in polymer solutions as demonstrated by

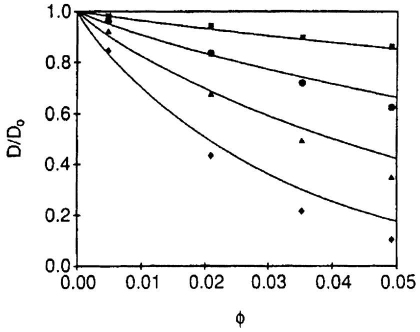

Fig. 3. Simulation of D/D_0 versus the polymer volume fraction for particles with 5 Å (squares), 12 Å (circles), 20 Å (triangles) and 30 Å (diamonds). The solid lines are the predictions with the hard sphere theory (Eq. (13)). Reprinted with permission from J Chem Phys 1993;98(9):7471. ©1999 American Institute of Physics [82].

several researchers [34–36,65]. An example is provided in Fig. 2. In addition, Eq. (10) does not provide diffusant size or shape dependence either, as in the case of Eq. (9) discussed in Section 2.1.1.

2.1.3. The model of Ogston et al.

In order to provide a theoretical explanation for the empirical equation of Laurent and coworkers [74,75], which relates the sedimentation of proteins in hyaluronic acid solutions, Ogston et al. [76] developed an approach for the diffusion of larger diffusants. The authors considered the polymer as barriers formed by a random distribution of long molecular fibers. Consequently, the self-diffusion coefficient for a given diffusant molecule depends both on the size of the obstacle present in the solution and on the size of the diffusant, as shown in the following equation:

$$\frac{D}{D_0} = \exp\left[-\frac{R_h + \rho}{\rho}\varphi^{1/2}\right] \tag{12}$$

where φ represents the volume fraction of the polymer, R_h the hydrodynamic radius of the diffusing molecule and ρ defines the effective cylindrical radius of the fiber. Diffusing molecules are considered as non-perturbing for the network. Therefore, this model should be applicable to polymer solutions and gels. Nevertheless, their data showed different results depending on the polymers employed (dextran and hyaluronic acid [77]. They attributed these differences to the morphology of the polymers, i.e. the rigidity and/or thickness of the polymer chains.

According to Johansson et al. [77], the differences observed by Ogston and coworkers were due to differences in the flexibility of the polymer chains. In a companion paper, they showed that the phenomenological approach of Ogston et al. [76] did not give consistent explanation in regard to their experimental results [31]. They demonstrated that the model of Ogston et al. remained valid for dilute or semi-dilute polymer solutions. This conclusion is in agreement with several other studies [26,38,78]. For example, Petit [78] showed that the model of Ogston et al. did not provide satisfactory results for large molecules despite the introduction of parameters related to the sizes of both the solute and the polymer. The deviation is more pronounced for concentrated polymer solutions.

2.1.4. Hard sphere theory

In order to expand the approach of Ogston et al. [76] to flexible polymers, Johansson and coworkers

Table 1
Summary of the diffusion models based on obstruction effect (Section 2.1) with their applicability and restraints

Author(s)	Reference(s)	Application(s)	Limitation(s)
Maxwell–Fricke	[25]	Solvents and small-sized diffusants Very dilute polymer solutions	Large diffusants Semi-dilute and concentrated polymer solutions
Mackie and Meares	[68]	Solvents and small-sized diffusants Semi-dilute polymer solutions	Large diffusants Concentrated polymer solutions
Ogston et al.	[76]	Solvents and small-sized diffusants Semi-dilute polymer solutions	Large diffusants Concentrated polymer solutions
Hard sphere theory	[31,79]	Solvents and small-sized diffusants Semi-dilute polymer solutions	Diffusants with $R_h > 20$ Å Concentrated polymer solutions

[31,79] elaborated a new diffusion model for spherical solutes in polymer solutions and gels. This model was based upon three main assumptions: (1) steric hindrance is the cause of the reduction of solute diffusion, and hydrodynamic interactions are negligible in the polymer solutions and gels; (2) the steric hindrance is caused by the static network, not by the interaction with diffusing species; (3) the structure of the network is decomposed into a set of cylindrical cells and the contribution from each cell to the diffusion coefficient is determined by the distribution of spaces in the network [31].

In this model, the hindrance due to the polymer chains is considered to depend not only on the size of the diffusant and the amount of polymer but also on the properties of the polymer chains, i.e. their thickness and stiffness [31]. Basically, they regarded the diffusion quotient, D/D_0, as the result of local flows in microscopic subsystems. Consequently, in order to quantify the hindrance of the polymer chains, the authors evaluated by the use of computational methods the closest distance (R) between a point in the network and the fiber, which is represented as a cylindrical cell. According to the computational modeling, the diffusion coefficient is given by

$$\frac{D}{D_0} = \mathrm{e}^{-\alpha} + \alpha^2 \mathrm{e}^{\alpha} E_1(2\alpha) \tag{13}$$

where α is a parameter related to the physical properties of both the polymer and the diffusant,

$$\alpha = \varphi \frac{(R_h + \rho)^2}{\rho^2} \tag{14}$$

where φ is the volume fraction of the network, ρ is the polymer radius and R_h the hydrodynamic radius of the diffusant. In Eq. (13), E_1 is an exponential integral:

$$E_1(x) = \int_x^\infty \frac{\mathrm{e}^{-u}}{u} \mathrm{d}u \tag{15}$$

Application of this model provided good results for the diffusion of albumin, $M \cong 69\,000$ Da [80], in hyaluronic acid and dextran solutions and gels, $\varphi = 0.004$ and 0.006, respectively [31]. Several simulations [81–83] of the hard sphere theory were made and limitations of the model were shown. For example, the theory failed when the authors attempted to simulate the self-diffusion coefficients of diffusants with increasing radius (5–30 Å) for a fixed polymer radius of 5 Å and a given persistence

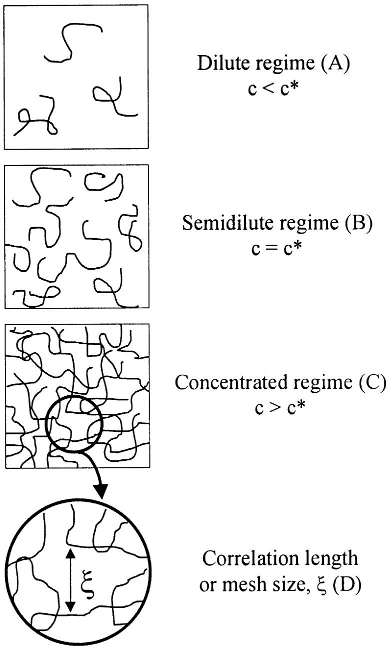

Fig. 4. Representation of the (a) dilute (b) semi-dilute and (c) concentrated regimes of polymer solution as well as the (d) correlation length in the concentrated regime.

length of 200 Å [81]. In fact, Eq. (13) does not fit Brownian dynamic simulations of spheres when the diffusant radius was above 20 Å (Fig. 3). Moreover, the authors were unable to provide an interpretation concerning the parameter α (Eq. (14)), which depends on the volume fraction and radius of the polymer as well as the hydrodynamic radius of the diffusant. The correlation between the theory and the simulation is good for low α, but discrepancy appears especially for higher values of α which correspond to large-sized diffusants [81]. The model also failed for nonionic micelles systems in ionic polymers [83].

Zhang and Lindman [84] reported the application of the obstruction model of Johansson and coworkers [31,79] for the diffusion of micelles in cellulose solutions ($\varphi < 2$ wt%). The obstruction due to the polymer was predicted correctly by the model. This diffusion study was carried out only in very dilute polymer concentrations. Bu and Russo [39] tried to interpret their diffusion data of dextran in 1 wt% hydroxypropyl cellulose solutions with the hard sphere theory, they found that the model of Johansson et al. [31,79] underestimated the diffusion coefficient at larger R_h. They concluded that the diffusants were structurally too complex to agree with Eq. (13). Other discrepancies with the hard sphere theory were also found in the literature [28,85].

2.1.5. Summary

It appears that all the obstruction effect models can fit self-diffusion coefficient data of small molecules in dilute or semi-dilute polymer solutions. We would like to point out that others theories, such as the models of Laurent et al. [86], Jönsson et al. [87], Hanai [88] and Phillips and Janssons [89] (see Fig. 2 for example) were also proposed. Their application is similar to those described in this section [37,64,90]. The uses and constraints for the models described in this section are summarized in Table 1.

Several self-diffusion studies in polymer solutions and gels have led to similar conclusions concerning the model of Mackie and Meares and the Maxwell–Fricke model [35,36,65]. The phenomenological approach of Ogston et al. [76] for larger molecules and the hard sphere theory failed at high polymer concentrations when hydrodynamic interactions became non-negligible [28]. In a study of self-diffusion in aqueous solutions of PVA, Petit et al. [34] demonstrated that the diffusion behavior of very small molecules such as water and methanol can be described by the obstruction models. But the same study showed that the theoretical prediction by the model of Mackie and Meares [68] deviates progressively from the experimental data with increasing diffusant size. Even for small diffusants, problems arose when the polymer concentration was high.

2.2. Hydrodynamic theories

The hydrodynamic theories take into account the hydrodynamic interactions present in the whole system. These interactions include frictional interactions between the solute and the polymer, likely the most important, between the solute and the solvent, and also between the solvent and the polymer. Such considerations allow the description of the diffusion in more concentrated regimes when the polymer chains start to overlap, which seemed difficult with the obstruction models.

2.2.1. Cukier's model

In 1984, Cukier [26] developed an equation to describe the diffusion of Brownian spheres in semi-dilute polymer solutions based upon hydrodynamic interactions. In this theory, the semi-dilute solution was considered as a homogeneous monomer unit environment as the polymer coils overlap, in comparison to the dilute solutions where the polymer chains do not interact with each other (Fig. 4(a)). In fact, the whole semi-dilute solution was viewed as a uniform solvent–polymer mixture. The dilute solution was considered as an inhomogeneous system composed of both polymer–solvent and pure solvent domains [26]. This semi-dilute solution of the polymer was approximated as motionless relative to the diffusing solvent, and represented by randomly distributed spheres immersed in an incompressible Navier–Stokes fluid. Thus, the diffusant was considered to undergo screening effects due to the overlapping of the polymer chains, and its diffusion coefficient as follows:

$$D = D_0 \exp(-\kappa R_\mathrm{h}) \tag{16}$$

where κ represents the screening hydrodynamic interactions between the polymer and the solute in a semi-dilute polymer solution, and R_h is the hydrodynamic radius of the diffusing sphere. The screening parameter relates the resistance of the polymer network to the diffusion of the remaining molecules, i.e. solvent(s) and diffusant particle(s). For dilute polymer solutions, assuming that screening remains dominated by hydrodynamic interactions, Eq. (16) can be rewritten as

$$\frac{D}{D_0} = 1 - \kappa R_\mathrm{h}. \tag{17}$$

Cukier compared screening effects between rod and coil polymer solutions for the diffusion of Brownian spheres of radius R, but basically no difference was found. In the case of rod-like polymer

Table 2
List of the parameters found in the literature for the hydrodynamic equations in the form of $D = D_0 \exp(-\alpha c^{\nu})$ (Section 2.2)

Author(s)	Reference	α	ν
Cukier	[26]	$\propto R_h^1$	0.5
Laurent et al.	[95]	$\propto R_h^1$	0.5
Freed and Edwards	[93]	$\propto R_h^1$	1
Brown and Stilbs	[96]	$\propto R_h^1$	1
de Gennes	[94]	$\propto R_h^1$	0.75
Altenberger et al.	[97]	$\propto R_h^0$	0.5
Ogston et al.	[76]	$\propto (R_h + \rho)/\rho$	0.5
Matsukawa and Ando	[98]	–	0.71

molecules, the screening parameter was found to have the following relationship:

$$\kappa_L^2 = \frac{\xi_L n_L}{\eta} \tag{18}$$

where ξ_L is the friction coefficient for one rod, n_L the number density of rod-like polymer molecules and η the solution viscosity. The rod friction coefficient depends on the length and diameter of the rod (L and b, respectively, with $L \gg b$):

$$\xi_L = \frac{6\pi\eta(L/2)}{\ln(L/b)} \tag{19}$$

Similar to Eq. (18), the dependence of the screening parameter for coil-like polymer molecules can be written as

$$\kappa_D^2 = \frac{\xi n_a^*}{\eta} = 6\pi n_a^* a \tag{20}$$

where n_a^* is the monomer number density and a the monomer radius.

In semi-dilute solutions and with small-sized diffusants (R_h smaller), a dependence was found with the polymer concentration: $\kappa \sim c^{\nu}$ with $\nu = 1/2$, but not with the geometric factors of the polymer.

This model was initially elaborated with theoretical considerations and calculations. It was employed often in the literature [40,91,92]. Mel'nichenko et al. [91] studied tracer self-diffusion of water in moderately concentrated hydrogels. The results were found to be in agreement with the theory. More recently, the same research group presented evidence that Cukier's model remained valid for water self-diffusion in polyacrylamide (PA) and silica gels [92]. These studies showed clearly the validity domain of Cukier's model: diffusion of small diffusants in semi-dilute networks, i.e. semi-dilute polymer solutions and slightly cross-linked gels. Limitations were shown when the model was used for large-sized diffusants such as polymers or proteins. For example, Park et al. [40] showed that Eq. (16) is not applicable for protein diffusion in PA gels. This conclusion was corroborated by the work of Lodge and coworkers [41,42] who studied the diffusion of linear and star-branched polystyrene in poly(vinyl methyl ether) (PVME) gels and by Johansson and co-workers [31,79], who studied diffusion of albumin in hyaluronic acid and dextran gels.

The screening parameter which was found proportional to the polymer concentration (c^{ν}) have been shown to vary in different studies [93,94] as noted by Cukier [26]. Freed and Edwards [93] obtained an exponent equal to 1 for c for an ideal chain, defined as a polymer chain in an undiluted polymer solution without entanglements. This result was re-examined by de Gennes [94], who described the stochastic motion of long flexible chains in good solvents and concluded that in such systems the diffusion coefficient should scale with $c^{3/4}$. Other studies listed in Table 2 reported values between 0.5 and 1.

All the studies showed that the self-diffusion coefficient of a diffusant in a polymer solution is closely related to the polymer concentration. However, the exponent of the polymer concentration dependence is not a simple constant value and disagreement remains.

2.2.2. The model of Altenberger et al.

Altenberger et al. [97] described the rigid body of the polymer as immobilized points randomly distributed in a solution. The solvent is considered as an incompressible Newtonian fluid, filling the space between these points. A small molecule present in the solvent will interact with these points which represent the network. Thus, the hydrodynamic interactions were represented by the friction with the stationary points. The mobility of a diffusant will depend on the concentration of the obstacle, i.e. the polymer. At low concentrations (dilute or semi-dilute regimes) the interactions are weak and the diffusion coefficient is given by

$$D = D_0 \exp(-\alpha c^{1/2}) \tag{21}$$

where α is a parameter depending on the diffusing particle, and c represents the number concentration of obstacle (the polymer). Eq. (21) is a generalization of a previous prediction elaborated by the same research group also based on hydrodynamic interactions [99]:

$$\frac{D}{D_0} = 1 - Ac^{1/2} - Bc + \cdots \tag{22}$$

where A is proportional to the diffusant radius, and B defines a constant that relates the interactions between the polymer network and the diffusant particle.

These two equations (Eqs. (21) and (22)) bear resemblance to the equations defined by Cukier (Eqs. (16) and (17)). Kosar and Phillips [100] demonstrated that Eqs. (16) and (21) are mathematically equivalent, although derived differently. But the authors predicted a larger validity domain than that of Cukier's (*higher obstacle concentration and/or for particles which interact strongly with the solvent*). Several studies showed that this model had similar limitations in its applications [40–42]. Petit et al. [34] also showed that these models were less satisfactory in the interpretation of diffusion data of large molecules such as PEG-4000 in PVA solutions. The motion of larger diffusants can happen on the same scale as the motion of the polymer networks [78]. The applicability of these two models seems to be limited to small molecules as in the case of the obstruction models (Section 2.1).

2.2.3. Phillies' model

A more phenomenological approach was used by Phillies [52,101,102] to describe the self-diffusion behavior of macromolecules (polymer and protein) self-diffusion over a wide range of concentrations. The stretched exponential equation was proposed based upon numerous experimental data from his own research as well as those from the literature [52]. According to his observations, the polymer

Table 3
Dependence of parameter α on the hydrodynamic radius of the diffusant obtained in the literature for Phillies' diffusion model (Section 2.2.3) $D = D_0\exp(-\alpha c^{\nu})$

Author(s)	Reference(s)	α	δ
Phillies	[52,101,102]	R_h^{δ}	0 ± 0.2
Phillies	[104]	R_h^{δ}/α_0	1
Park et al.	[40]	$3.03 \times R_h^{\delta}$	0.59
Gibbs and Johnsson	[113]	$3.2 \times R_h^{\delta}$	0.53
Russo et al.	[114]	R_h^{δ}	0
Yang et al.	[115]	$R_h^{\delta}M^{0.76}$	0
Furukawa et al.	[46]	$MP^{1/2}$	–

self-diffusion coefficient obeys a scaling law

$$D = D_0\exp(-\alpha c^{\nu}) \tag{23}$$

where α and ν represent the scaling parameters which should depend on the molecular weight of the diffusant polymer. Experimentally, α was found to depend on the diffusant molecular weight ($\alpha \sim M^{0.9\pm0.1}$) for macromolecules, whereas α depends on the diffusant hydrodynamic radius ($\alpha \sim R_h$) for smaller molecules [102,104,105]. The scaling parameter ν should scale between 1 for low molecular weight diffusant and 0.5 for high molecular weight diffusant [101]. Inside these limits $\nu \sim M^{-1/4}$ [101]. Phillies considered the three regimes of concentrations (Fig. 4) defined for reptation theories, i.e. dilute solution where polymer chains move independently, semi-dilute solutions where polymer chains start to overlap, and concentrated solutions where diffusion is dominated by polymer friction. These regimes can be regarded as close to the polymer solutions examined by Cukier (Section 2.2.1), where forces in solution were defined as predominantly hydrodynamic for the last two regimes (Fig. 4(b) and (c)). Nevertheless, an important difference between this model and the models of Cukier [26] and Altenberger et al. [97] is that the polymer chains are regarded here as mobile and are described as spheres joined by rods that can rotate as defined by Kirkwood and Riseman [103].

In his following publications, Phillies developed theoretical arguments for Eq. (23) [101,102]. The stretched exponential equation is based on the following assumptions: (1) *the self-similar effect of infinitesimal concentration increment on D*; (2) *the functional form for hydrodynamic interactions between mobile polymer chains*; (3) *the dependence of chain extension on polymer concentration* [101].

The first assumption means that an infinitesimal increase of the concentration dc increases the drag coefficient of the diffusant from f to $f + K\mathrm{d}c$ (K may be concentration dependent). This assumption is based on the fact that the polymer self-diffusion coefficient is related to its drag coefficient, f, by the Einstein relation

$$D = \frac{k_B T}{f} \tag{24}$$

where k_B is the Boltzmann constant and T the temperature. The polymer should retard the diffusant and increase the drag. The drag coefficient of the solution that already retards the diffusant particle should be more important. The second assumption considers that the polymer–polymer interactions are mainly in hydrodynamic modes rather than in entanglement modes. Nevertheless, Eq. (23) does not provide a

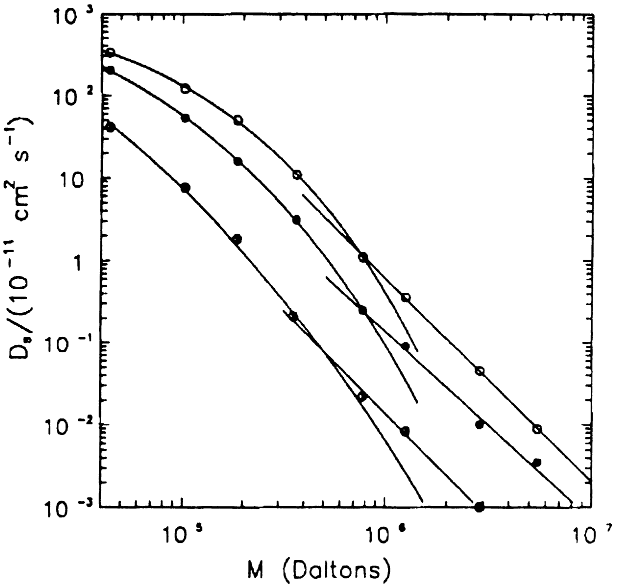

Fig. 5. Logarithmic plots of self-diffusion coefficients of PS in dibutyl phthalate as a function of the molecular weight of PS at various polymer concentrations: 13 g% (open circles), 18 g% (filled circles) and 40.6 g% (half-filled circles). Curved lines represent fittings to the stretched exponential equation (Eq. (23)) while straight lines correspond to power laws. Reprinted with permission from J Phys Chem 1992;96:10061. ©1999 American Chemical Society [117].

screening effect parameter because the polymer chains were regarded as mobile, thus no fixed sources of frictional interactions were present in the solution. In fact, polymer chains in solution will reduce both the flow rate and the molecular diffusion as the chains rotate. Moreover, the polymer chains will create an echo phenomenon responsible for fluctuation on the whole polymer system. The final approximation, based on Daoud law [106] for a large polymer in semi-dilute regimes, stipulates that the polymer chains contract under the overlap concentration: $R_g^2 \approx Mc^{-x}$ where x is a parameter. As results of these presumptions, ν fluctuates between 1/2 for large polymers to 1 for small polymers, and inside these limits, $\nu \sim M^{-1/4}$ for a given diffusant [101]. Macromolecular self-diffusion coefficient can be described by the stretched exponential equation (Eq. (23)) with $\alpha \sim M$ and ν as stipulated above [101].

Such an equation has already been employed to describe other physical transport phenomena such as sedimentation of large colloidal particles through a semi-dilute polymer solution [107], electrophoretic mobility [43] and viscosity [108]. Thus, Eq. (23) can be considered as a “universal” equation, as named by Phillies, because it can be employed for different physical transport phenomena. This equation is very flexible in nature. Walderhaug et al. [44] and Wheeler and Lodge [45] pointed out that it should be regarded as an empirical equation.

Phillies investigated the applications of the universal equation to numerous experimental data from the literature and found good agreements of the equation with the data for various polymer systems [101,109,110]. Similarly, several publications showed excellent fittings of the experimental data with Eq. (23) [40,45–48,111,112]. These articles reported the diffusion of large diffusants in dextran gels [46,47], PA gels [40], associative polymers [48,112], and the diffusion of linear and star branched PS in PVME gels [45,111] over large ranges of concentrations. In addition, this equation was also employed successfully to describe self-diffusion data of small diffusants in PA gels [40] and in PVA solutions and gels [34]. However, Won et al. [49] reported deviations from the equation for PS sphere tracer diffusion in PVME solutions at higher concentrations.

It was argued, however, that the physical significance of the parameters α and ν in the various systems remains vague, and the lack of theoretical justifications was underlined in the literature [34,40,43–51]. Phillies suggested that α varies with R_h/a_0 for the polymer diffusant, where R_h is the hydrodynamic radius of the diffusant and a_0 is defined as the distance of closest approach between the solute and the polymer bead [104]. Other estimations of α led to slightly different results as shown in Table 3. Masaro et al. [116] used Eq. (23) to analyze the diffusion data of PEG in PVA solutions and gels. Eq. (23) provided good fittings to the experimental data, but attempts to relate the scaling parameters with the physical properties of the system (such as diffusant size) were not successful. These results are corroborated by several reports in the literature [34,40,43–51]. An example is provided in Fig. 2. In addition, analyses of the variable temperature diffusion data showed that the scaling parameters are not temperature-dependent. An Arrhenius dependence of D_0 on the temperature was found. The results are different from the temperature dependence of the scaling parameters found by Phillies.

Recently, Phillies et al. [105,117] reported the applicability of this hydrodynamic scaling model for high molecular weight polymers over small and large concentrations. From these studies, it seems clear that the stretched exponential form can fit easily diffusion data in solution-like systems whereas a power law is more appropriate to fit diffusion data in melt-like systems, which correspond to very concentrated polymer solutions. The boundary between solution-like to melt-like systems was estimated to be in the order of $M \approx 10^6$ g/mol in the case of polystyrene (Fig. 5) [117].

2.2.4. The reptation and reptation plus scaling models

The reptation theory was first introduced by de Gennes [118] who discussed the self-diffusion of a polymer chain of molecular weight M moving inside a three-dimensional network of polymer chains of molecular weight P, which is considered as a gel. This theory was complementary to the works of Rouse [119] and Zimm [120], who had studied the stochastic motion of a single polymeric chain dissolved in a solvent of low molecular weight [118].

In the reptation theory, the diffusing polymer chain is regarded as constrained by fixed obstacles that represent the gel chains. As the polymer chain is surrounded, the leading motions of the polymer chain are feasible only at the extremities. Thus, the motion of the central part of the polymer chain takes place when the extremity enters inside a new tube. Consequently, the central part of the polymer chain remains confined between the same fixed obstacles for a longer time in comparison to the extremity of the polymer chain. Thus, this part of the polymer chain is said to remain in a tube formed by the neighboring polymer chains [121]. Therefore, only “tubular” motion is conceivable and lateral motion is not considered, as the diffusant polymer is enveloped by the network. Brownian motion for high molecular weight polymers in the tube was predicted to depend on their molecular weight [118]:

$$D \sim M^{-2}. \tag{25}$$

The diffusion of a high molecular weight polymer in an unentangled system, or a diluted solution, is described by the Rouse model [119]:

$$D \sim M^{-1}. \tag{26}$$

Table 4
Experimental values obtained for the dependence on the molecular weight (*M*) of the diffusant and polymer concentration (*c*) in de Gennes' reptation models (Section 2.2.4)

Author(s)	Reference(s)	Description	Result
Reptation model: $D \sim M^{-2}$ and $D \sim M^{-1}$			
Klein	[139]	Polyethylene in bulk	$D \sim M^{-2}$
Bartels et al.	[140]	Polybutadiene in bulk	$D \sim M^{-2}$
Fleischer[a]	[141]	PS self-diffusion by NMR	$D \sim M^{-2}$
Kumagai et al.	[142]	PS in bulk	$D \sim M^{-2.7}$
Smith et al.	[143]	Poly(propylene oxides)by fluorescence photobleaching	$D \sim M^{-1.7}$
Antonietti et al.	[144]	PS by forced Rayleigh scattering	$D \sim M^{-2.2}$
Wheeler and Lodge	[45]	PS in PVME/o-fluorotoluene	$D \sim M^{-0.56 \sim -2.3}$
Yu et al.	[56,57]	PS in THF	$D \sim M^{-2}$
		PS in toluene (no concentration scaling)	$D \sim M^{-3}$
Reptation plus scaling model: $D \sim M^{-2}c^{-1.75}$ and $D \sim M^{-2}c^{-3}$			
Léger et al.	[127]	PS in benzene	$D \sim M^{-2}c^{-1.75}$
Schaefer et al.	[145]	Marginal solvent	$D \sim M^{-2}c^{-2.5}$
Wheeler and Lodge	[45]	PS in PVME/o-fluorotoluene	$D \sim c^{-3.3}$
von Meerwall et al.	[130]	PS in THF Without correction for local friction	$D \sim M^{-1.5}c^{-1.75}$
Cosgrove et al.	[53]	PS in CCl_4	$D \sim c^{-2.25}$
Callaghan and Pinder	[146]	PS in CCl_4	$D \sim M^{-1.4}c^{-1.75}$
Manz and Callaghan	[147]	PS in cyclohexane	$D \sim c^{-2}$

[a] Also valid for molecular weight less than the critical molecular weight, M_c, observed in the melt viscosity.

Several years later, de Gennes [122] reexamined the reptation theory in order to introduce the scaling concepts. He took into account of the effect of the matrix on the self-diffusion coefficient of the diffusant. This reexamination led to a new model, the *reptation plus scaling* concept, which is defined by the following equation [122,123]:

$$D \sim M^{-2}c^{(2-\nu)/(1-3\nu)} \tag{27}$$

where M is the molecular weight of the diffusant, c the polymer matric concentration and ν the Flory exponent for the excluded volume.

Eq. (27) leads to two distinct equations for diffusion in the semi-dilute regime, one for good solvents ($\nu = 3/5$)

$$D \sim M^{-2}c^{-1.75} \tag{28}$$

and the second for θ solvents ($\nu = 1/2$)

$$D \sim M^{-2}c^{-3}. \tag{29}$$

The θ solvent regime corresponds to an exact cancellation between steric repulsion and van der Waals attraction between monomers [123]. Thus, the polymer chains do not overlap in θ solvents. This regime corresponds to $c < c^*$ (Fig. 4(B)), where c^* is defined as the critical overlap concentration. In the good solvent regime, the polymer chains tend to swell. Therefore, the polymer chains are densely packed and start to overlap, which corresponds to the concentrated regime, $c > c^*$ (Fig. 4(C)).

Applications of de Gennes' diffusion models are numerous in the literature. Léger et al. [121] showed that the dynamics of a linear chain could be described by simple reptation (Eq. (25)). The same correlation was reported by Gent et al. [124,125], who studied diffusion of *cis*-1,4-polyisoprene into *cis*-polyisoprene networks, and by Antonietti and Sillescu [126], who studied PS self-diffusion in bulk PS network by holographic grating technique. Previously, Léger et al. [127] studied the self-diffusion of labeled PS chains in unlabeled PS chains of the same molecular weight in benzene by forced Raleigh scattering and found reasonable agreement with Eq. (28). Similar results were obtained by Kim et al. [128] who studied the diffusion of styrene–acrylonitrile copolymers by recoil spectrometry, Pajavic et al. [129] who studied the diffusion of linear polyelectrolyte in gels by dynamic light scattering and von Meerwall et al. [130] who studied PS self-diffusion in tetrahydrofurane by NMR for a concentration above the entanglement concentration and after correction for local frictions. Recently, this model was also employed to explain the disentanglement of polymeric chains during dissolution which led to the definition of a mathematical model for polymer dissolutions [131,132]. The reptation theory was also used for the electrophoretic separation of DNA in gels [38,133–135]. The theoretical treatments of the motion of DNA through gels are mainly based on the reptation model. The DNA is pictured as moving through an impenetrable tube defined by the surrounding gel obstruction, with the motion mediated by a snake-like reptation of the polymer ends [133].

Phillies [52] pointed out that the use of Eqs. (25) and (26) to describe diffusion does not allow an exponential decrease of the diffusant self-diffusion coefficient with respect to the polymer concentration which was frequently observed [34,36,65,136]. The reptation model led to two distinct regions as shown by Eqs. (28) and (29), one for each concentration regime: $c < c^*$ and $c > c^*$ (Fig. 4(b) and (c)). The original reptation model of de Gennes considers that the entanglement of the polymer chains occurs at the critical overlap concentration c^*. However, Kavassalis and Noolandi [137,138] have predicted that the entanglement concentration, c_e, is about 10 times higher than the overlap concentration. In the work of Cosgrove et al. [53,54], the reptative exponent of -2 (Eq. (25)) was not found even for high polymer concentrations but the spin–spin NMR relaxation time and viscosity measurements showed the presence of chain entanglements. Nemoto et al. [55] reported studies of concentrated solutions of linear PS self-diffusion in dibutyl phthalate (M_w from 6180 to 2 890 000). They interpreted their data by the use of the reptation model (Eqs. (25) and (26)) and found good agreement with the model of Rouse (M^{-1}) for low concentrations whereas a power law of $M^{-2.6}$ was found for concentrated solutions instead of M^{-2}. In the study of linear PS (M_w from 32 000 to 1 050 000) diffusion in PVME gels, Rotstein and Lodge [41] reported a power law of $M^{-2.8}$. Yu and coworkers [56,57] studied diffusion of labeled PS chains (M_w from 32 000 to 360 000) in unlabeled PS–THF systems (with $P = M$), and diffusion of labeled PS chains (M_w from 10 000 to 1 800 000) in PS–toluene systems (with $P/M \geq 3.5$). In both cases, the authors did not observe any concentration scaling. The results from the use of de Gennes' models are summarized in Table 4. In a recent work, Cheng et al. [149] studied self-diffusion of poly(ethylene oxide) in the melt as a function of the temperature. They showed that the power dependence for high molecular weight diffusants varied between $M^{-2.24}$ (353.7 K) and $M^{-2.75}$ (413.7 K). These values are not in good agreement with the prediction of de Gennes (Eq. (25)) and indicate that de Gennes' reptation model cannot be used to describe the temperature dependence of the diffusion in polymer systems. In

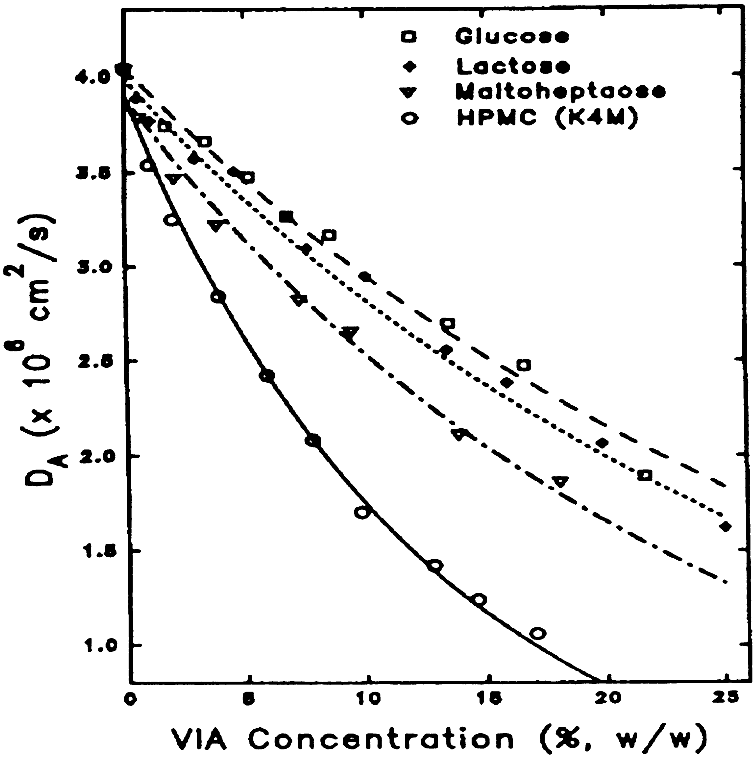

Fig. 6. Plot of the self-diffusion coefficients of adinazolam as a function of the VIA concentration (w/w, %). The adinazolam concentration is kept constant for each series. Squares, 0.5% Adinazolam plus *x*% glucose; Diamonds, 0.5% Adinazolam plus *x*% lactose; Triangles, 0.5% Adinazolam plus *x*% malteose; and circles, 0.5% Adinazolam plus *x*% HPMC. Fitting are obtained by the use of Eq. (32). Reprinted with permission from Pharm Res 1995;12:955. ©1999 Plenum Publication Corporation [32].

addition, Wheeler and Lodge [45] studied linear and branched PS diffusion in PVME/*o*-fluorotoluene solutions and observed a large variation of the scaling exponent varying from $M^{-0.56}$ to $M^{-2.3}$ with changes in the matrix concentration, which demonstrate that a simple power law equation is not sufficient to describe the diffusion process. In the same study, Wheeler and Lodge have studied the concentration effect. In concentrated polymer solutions they observed a power dependence of $c^{-3.3}$, close to the predicted value of c^{-3}, whereas in semi-dilute solutions the predicated $c^{-1.75}$ scaling was not observed. Marmonier and Léger [148] noticed that the diffusion coefficient depends on P when the factor P/M is greater than 5.

The limitations in the application of the reptation model were discussed in several publications by Phillies [52,101,102]. The main conclusion was that *reptation is probably not important for polymer self-diffusion in solution* [101]. However, de Gennes' model succeeded in the interpretation of results of diffusion of linear and branched polymers in concentrated polymer matrix solutions [45,111], DNA diffusion [38], polymer dissolution [132], etc. However, some important points should be addressed since no comprehensive illustration based on a molecular theory explains the entanglement phenomenon (the nature of an entanglement and the criteria for the onset of entanglement effects are not established), and no clear explanation concerning the reptation of a single linear chain in dilute solution has been provided yet [42,150].

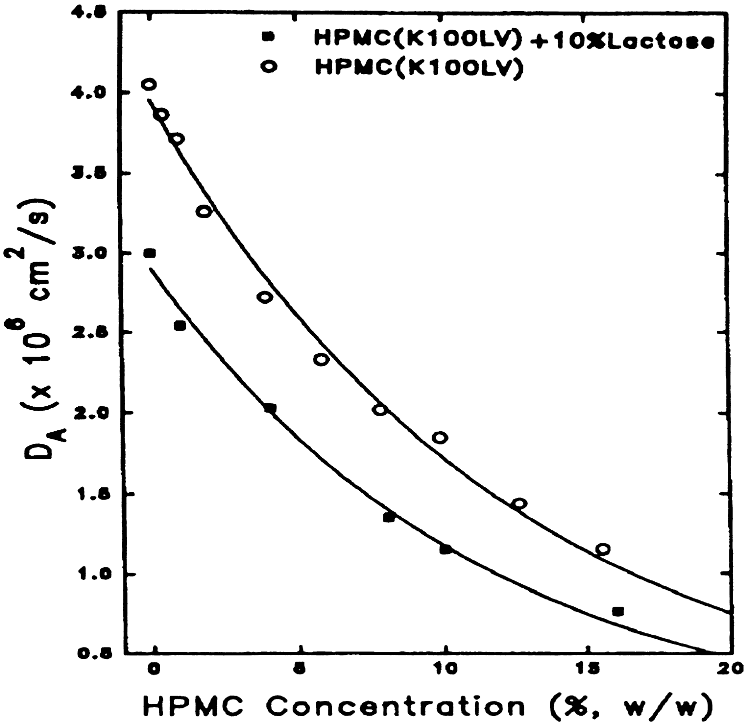

Fig. 7. Plot of the self-diffusion coefficients of adinazolam as a function of HPMC concentration (w/w, %). Open symbols represent the data for 0.5% Adinazolam plus *x*% HPMC, and filled symbols represent the data for 0.5% Adinazolam plus 10% lactose and *i*% HPMC. Fittings are obtained by the use of Eq. (32). Reprinted with permission from Pharm Res 1995;12:955. ©1999 Plenum Publication Corporation [32].

2.2.5. The model of Gao and Fagerness

This model is based on measurements of drug (adinazolam) and water diffusion in hydroxypropyl methyl cellulose (HPMC) gels studied by NMR spectroscopy [32]. The authors did not elaborate on hydrodynamic arguments, but the form of the equation is very similar to the form of the equations based on hydrodynamic theories.

Gao and Fagerness [32] observed exponential decrease of both adinazolam and water diffusion with increasing HPMC concentration. Furthermore, using different HPMC gels with different viscosity grades (100, 4000, 15 000 cps), i.e. different molecular weights, they did not observe any effect on the diffusion process. Diffusion measurements in HPMC gels were also carried out in the presence of glucose, or lactose, or maltoheptaose (monomer, dimer and oligomer of the HPMC, respectively), which were defined as viscosity-inducing agent (VIA) [32]. A significant decrease in the adinazolam self-diffusion coefficient was reported with increasing the size of the VIA in the adinazolam–water–VIA ternary solutions.

Thus, the self-diffusion coefficient of adinazolam was found to depend on the nature of the VIA present in solution as well as on its concentration as illustrated in Fig. 6. This dependence can be described by an exponential function of the VIA concentration

$$D = D_0 \exp(-K_i c_i) \qquad (30)$$

Table 5
Summary of the diffusion models based on hydrodynamic theories (Section 2.2) with their applicability and restraints

Author(s)	Reference(s)	Application(s)	Limitation(s)
Cukier	[26]	Solvents and small-sized diffusants	Large diffusants
		Semi-dilute polymer solutions and highly swollen gels	Concentrated polymer solutions
Altenberger et al.	[97]	Solvents and small-sized diffusants	Large diffusants
		Semi-dilute polymer solutions	Concentrated polymer solutions
Phillies	[52,101,102]	Solvents, small-sized diffusants and macromolecules	Significance of the scaling parameters
		Diffusion in solution-like regimes	Diffusion in melt-like regime ($M > 10^6$)
de Gennes	[122,123]	Diffusion of macromolecules in gels and concentrated polymer solutions	Molecular significance of entanglements
			Theoretical prediction not observed even for $c > c^*$
Gao and Fagerness	[32]	Diffusion of small-sized diffusants in multicomponant systems	Significance of the main parameters

where D is the self-diffusion coefficient of adinazolam, i represents the VIA, K_i is a proportionality constant and c_i the concentration of VIA. K_i values for adinazolam were obtained by a linear least square fit of the diffusion data from binary systems. For example, K_{glucose} is obtained from the diffusion data of glucose–water binary solution.

Gao and Fagerness [32] examined also drug diffusion in VIA mixtures. Their results indicated that drug diffusivity in a multi-component system (HMPC and lactose) was influenced by all the components present in the system: VIA, polymer and even the drug concentration (Fig. 7). This result led to a re-examination of Eq. (30)

$$D = D_0 \exp(-K_H c_H - K_L c_L - K_A c_A) \tag{31}$$

where c_H, c_L and c_A are the concentrations of HPMC, lactose and the drug (adinazolam), respectively.

Good agreement was found between the measured and the calculated self-diffusion coefficients over a wide range of HPMC concentrations (0–30 wt%). Water self-diffusion coefficient was also determined and a dependence on the VIA concentration was also found. However, water showed the same concentration dependence whichever VIA was employed, individually or mixed. These results were consistent with the observations above and lead to the final form of the model [32]

$$D = D_0 \exp\left(-\sum K_i c_i\right). \tag{32}$$

Variable temperature experiments were done between 10 and 50°C. The activation energy of drug diffusion, E_a, was determined in each of the solutions with a fixed concentration of VIA. The same Arrhenius behavior was observed in these cases, leading to a similar E_a. A comparable result was obtained with water diffusion over the same temperature range [32].

If we consider the specific case of a ternary solution of low concentration of the diffusant ($c_D \ll c_H$) plus solvent and HPMC, the self-diffusion coefficient of the drug will depend only on the polymer concentration according to this model. Thus the diffusion coefficient can be written as

$$D = D_0 \exp(-K_H c_H) \tag{33}$$

which is similar to the equation defined by Freed and Edwards [93] for an ideal chain, with $K_H \sim R_h$

$$D = D_0 \exp(-R_h c). \tag{34}$$

Moreover, Eq. (33) represents also a particular circumstance of Phillies' stretched exponential equation with $\nu = 1$ (Section 2.2.3).

This model provided good agreements for the diffusion of small molecules such as a drug and water in multi-component systems over a wide range of concentrations at different temperatures. However, the authors did not explain the importance of the proportionality constant, K_i, neither its physical significance nor its dependence on the polymer molecular weight and/or diffusant size. In addition, no relationship between the diffusion coefficient and the temperature was provided.

In a companion paper, Gao et al. [151] tried to make predictions of drug release rates in polymer tablets. To reach this goal, they used the Higuchi equation [152] in which they introduced their diffusion model, Eq. (32), assuming that *the formulations exhibit identical swelling kinetics* (*medium penetration rate, matrix swelling and erosion*) *and that the concentration of drug and VIA in the gel layer are proportional to their respective weight concentration in the dry tablet.* However, no good agreement was found between the experimental results and the theoretical prediction, although the agreement was good in the previous self-diffusion study. This work demonstrated that diffusion in swollen and equilibrated gel is quite different from the drug release from a dry tablet. The self-diffusion studies of already equilibrated systems may be quite different from real time situations such as the release of drugs. It is important to establish correlations between these two diffusion processes.

2.2.6. Summary

The major advantages and constraints for the models described in this section are summarized in Table 5.

The models of Cukier [26] and Altenberger et al. [77], where the polymer chains are regarded as motionless, can be used to describe the diffusion of small-sized diffusant in semi-dilute polymer solutions. These models cannot be employed to describe solute diffusion in concentrated polymer solutions.

The universal equation proposed by Phillies is a useful equation (simple form, good correlation with experimental data) to fit diffusion data of both small-sized diffusants and macromolecules in all concentration regimes, excepted for melt-like region. This model has a simple equation form which generally provides good fittings to the experimental data. Further improvements were reported by Phillies and coworkers on temperature effect [153], glass transition temperature dependence [154], diffusion under θ and good solvent conditions [155], a reanalysis of the stretched exponential equation [156], and justifications [157–159]. However, some applications of the model remained obscure, temperature variation was not supported and the interpretations of the scaling parameters was sometimes contested, even though complementary justifications have been published recently [160].

The reptation model was first introduced to describe diffusion in gels but can also be used in some cases for polymer solutions [125–128]. It seems that its application is successful in cross-linked gels, concentrated polymer solutions and melts. It cannot be used in semi-dilute polymer solutions, especially when the entanglement concentration is not reached [116]. The use of the reptation equations (Eqs. (25), (26) and (27), (28)) to describe diffusion with respect to the polymer concentration does not reproduce the exponential dependence observed experimentally. In addition, the model cannot describe the temperature dependence, and discrepancy was underlined concerning the concentration exponent dependence and the theoretical predictions, as shown in Table 4.

The main advantage of the model of Gao and Fagerness [32] is that the diffusant concentration is also taken into account. The physical significance of the parameters in this model needs to be elucidated. No other application of the model was found in the literature due to novelty of the model.

2.3. Diffusion models based on the free volume theory

The free volume concept in polymer science is well known. The free volume was defined as the volume not occupied by the matter. More generally, the free volume can be specified as the volume of a given system at the temperature of study minus the volume of the same system at 0 K. Thus, rearrangement of the free volume creates holes through which diffusing particles are able to pass through. The free volume is contributed by all the species present in the system, solvent, solute(s) and polymer. The free volume theories are based on the assumption that the free volume is the major factor controlling the diffusion rate of molecules.

2.3.1. Fujita's model

The first diffusion model based on free volume theory was proposed by Fujita [27]. The measurements were carried out in a ternary system including a solvent, a polymer and a penetrating molecule (a plasticizer). The concentration of the plasticizer was kept low, in comparison with the polymer concentration, thus the system could be approximated as a pseudo-binary system. Therefore, the average free volume in such a system was contributed by the polymer and the solvent. In order to estimate the free volume, Fujita used the concept of Cohen and Turnbull [161] which defines the probability $P(\nu^*)$, to find holes of size ν^* in a liquid of identical molecules

$$P(\nu^*) = A \exp\left(-\frac{b\nu^*}{f_V}\right) \tag{35}$$

where A is constant, b a numerical factor of the order of unity and f_V is the average free volume per molecule. The product $b\nu^*$ is interpreted as the measure of the minimum hole size required for diffusant displacement B. The diffusion model is based on several assumptions: (1) the diffusion process occurs because of the redistribution of the free volume within the matrix; (2) the redistribution of the free volume does not require energy change; (3) the diffusion process is enabled when the free volume exceeds holes of size ν^*; (4) the diffusion is directly proportional to the probability $P(\nu^*)$ of finding a hole of volume ν^* or larger adjacent to the diffusant molecule [161].

Fujita assumed that Eq. (35) was valid also in the case of a binary system. Further, the probability that the molecule found in its surrounding a hole large enough to permit displacement is closely linked to the diffusant mobility, m_d

$$m_d = A \exp\left(-\frac{B}{f_V}\right) \tag{36}$$

where A is a proportionality factor and B depends only on the particle size but not on the temperature or on the polymer concentration. The definition of the mobility is given by

$$D = \mathrm{R}Tm_d \tag{37}$$

where D is the self-diffusion coefficient of the molecule, T is the temperature and R the gas constant.

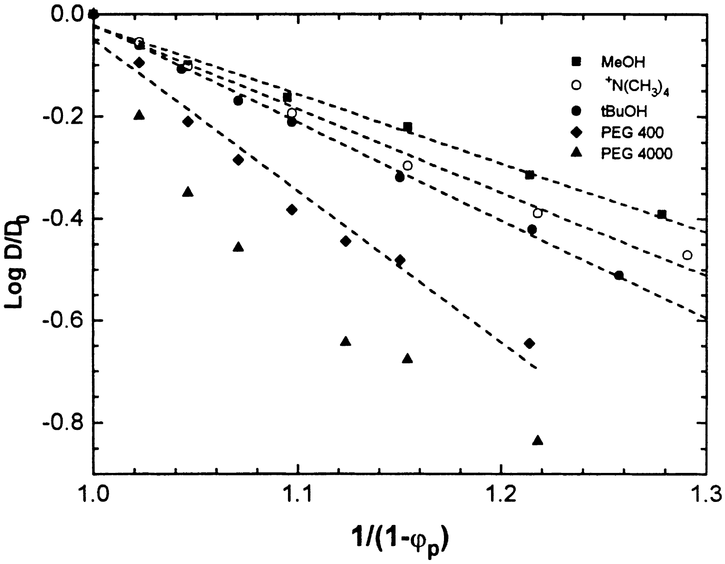

Fig. 8. Semilogarithmic plot of the normalized self-diffusion coefficient of various diffusants as a function of $1/(1-\varphi_p)$, φ_p being the polymer volume fraction. The dotted lines are fittings to Yasuda' free volume model (Eq. (40)). Reprinted with permission from Macromolecules 1996;29:70. ©1999 American Chemical Society [34].

Finally, substituting Eq. (36) into Eq. (37), we have

$$D = A\mathrm{R}T\exp\left(-\frac{B}{f_V}\right). \tag{38}$$

The application of Fujita's free volume theory showed successful correlations between the model and the data in the case of the diffusion of small molecules in semi-crystalline polymers [162]. Stern and coworkers [163,164] used Eq. (38) to fit their data of gas diffusion in polyethylene membranes and concluded that Fujita's model was applicable when the penetrant volume fraction was less than 0.20. Zhu et al. [165,166] showed that self-diffusion of ketone and ester solvents of various sizes and shapes in PMMA solutions can be well described by Fujita's free volume model. Similar results of solvent or tracer diffusion in polymer solutions and gels have appeared in the literature [46,167–169].

According to Fujita [27], the free volume theory provided a good agreement with polymer–organic-solvent systems whereas polymer–water systems failed because of the numerous interactions between the molecules. This conclusion was also reported by others in the literature [164,170]. Recently, Matsukawa and Ando [98] studied PEG diffusion in poly(*N*,*N*-diethylacrylamide)–water system. They showed that Fujita's equation fitted well water diffusion data, whereas for macromolecules such as PEG, the diffusion data was better described by de Gennes' reptation theory. In addition, Xia and Wang [165] showed that Fujita's model is valid only for low polymer volume fractions. Fujita's free volume model seems adequate in the description of the diffusion of small-sized diffusants in dilute and semi-dilute polymer solutions and gels, mostly organic systems.

2.3.2. The model of Yasuda et al.

Yasuda et al. [171] examined the free volume theory of diffusion assuming that the free volume of a binary system, as proposed by Fujita [27], mostly depends on the volume fraction of the solvent. This assumption was based on the fact that: (1) the polymer was less mobile than the solvent; (2) the effective free volume was considered mainly as a contribution from the solvent; (3) in practice, the solvent diffusion decreased with increasing polymer concentration. Therefore, the total free volume comes form the contributions of both the solvent and the polymer

$$f_v = \varphi_s f_s + (1 - \varphi_s) f_p = f_p + \varphi_s (f_s - f_p) \tag{39}$$

where f_v is the total free volume, f_s the free volume contribution from the solvent, f_p the free volume contribution from the polymer, φ_s the volume fraction of the solvent and φ_p the volume fraction of the polymer.

Substituting Eq. (39) into Eq. (38), and assuming that there is no interaction between the polymer and the diffusing molecule, we can obtain

$$\frac{D}{D_0} = \exp\left[\frac{B}{f_V^*}\left(1 - \frac{1}{1 - \varphi_p}\right)\right] \tag{40}$$

where f_v^* is the solvent free volume in the polymer solution.

Yasuda et al. [171] used the free volume theory to treat electrolyte (NaCl) diffusion in polymer systems. They used several swellable polymers derived from methacrylate, such as methyl, hydroxypropyl and hydroxyethyl methacrylate as well as cellulose in different solvents (dioxane, acetone, ethylene glycol, and water mixed with formic acid). The dependence of the diffusion coefficient on the volume fraction of water can be described by this model [171]. Matsukawa and Ando [172] studied water diffusion and used this model with success. Other sources of agreement were found in the work by Chen and Lostritto [173] who studied drug diffusion (benzocaine, with size smaller than the gel mesh size) in highly swollen poly(ethylene-co-vinyl acetate) membranes. Gilbert et al. [174] studied protein diffusion (lysozyme, ovalbumin, bovine serum albumin and carbonic anhydrase) in collagen membrane with glass diffusion cells and obtained results in good agreement with the model of Yasuda et al. [171]

Petit et al. [34,78] who studied diffusion of various diffusants in PVA–water systems demonstrated that this model works well for small diffusants but gradually deteriorates with increasing molecular size of the diffusants (such as oligomers and polymers) especially at high polymer concentrations (Fig. 8). Similar results were reported by Amsden [28]. Hennink and coworkers [58] studied protein diffusion in derivatized dextran hydrogels (chemically cross-linked). Their results showed disagreement between the data and the theory when the diffusant size is close to the hydrogel mesh size. In this case, screening effects started to occur which are not taken into account by the free volume concept. Therefore, the model of Yasuda et al. [171] can be used to analyze the diffusion data of relatively small-sized diffusants in dilute and semi-dilute polymer systems.

2.3.3. The model of Vrentas and Duda

A major contribution to the development of free volume theory was made by Vrentas and Duda [175–178] and coworkers [179–181] who re-examined and improved the free volume model over the years. They extended the free volume theory to a wide range of temperatures and polymer concentrations [182]. The free volume contributions from both the solvent and the polymer are taken into account. Therefore, Fujita's free volume model [27] appeared as a special case of the newer model of Vrentas and Duda [182]. With the numerous improvements, the free volume theory of Vrentas and Duda takes account of several physical parameters such as the temperature, the activation energy, the polymer concentration, the solvent size, and the molecular weight of the diffusant. In the case of a binary system (solvent diffusion in a polymer network) the model of Vrentas and Duda is expressed by the following equation:

$$D = D_{01}\exp\left[-\frac{E}{\mathrm{R}T}\right]\exp\left[-\frac{\omega_1\hat{V}_1^* + \omega_2\xi\hat{V}_2^*}{K_{11}\omega_1(K_{21} - T_{g1} + T)/\gamma_1 + K_{12}\omega_2(K_{22} - T_{g2} + T)/\gamma_2}\right] \tag{41}$$

where D_{01} is the solvent self-diffusion coefficient in the absence of polymer or a constant preexponential factor, E is the activation energy for a solvent jump, ω_i is the weight fraction of component i, $\hat{V}_1^*$ is the specific volume needed for one jumping unit of component i, ξ is the ratio of the volume of solvent jumping unit to that of the polymer jumping unit, γ_i represents the overlap factor for the free volume for pure component i, T_{gi} is the glass transition temperature of component i, K_{11} and K_{21} are the solvent free volume parameters and K_{21} and K_{22} are the polymer free volume parameters. The free volume parameters K_{11} and K_{21} were defined as follows:

$$K_{11} = \hat{V}_1^0 T_{g1}[\alpha_1 - (1 - f_{H1}^{G})\alpha_{c1}] \tag{42}$$

$$K_{21} = \left[\frac{f_{H1}^{G}}{\alpha_1 - (1 - f_{H1}^{G})\alpha_{c1}}\right] \tag{43}$$

where α_1 is the thermal expansion coefficient of the solvent, α_{c1} is the thermal expansion coefficient for the sum of the specific occupied volume and the specific interstitial free volume, $\hat{V}_1^0$ is the free volume occupied by the solvent at 0 K, and f_{H1}^{G} is the average fractional hole free volume.

The approach of Vrentas and Duda is based on the following assumptions: (1) the mixing of the polymer and solvent partial specific volumes does not lead to volume change; (2) the polymer thermal expansion coefficients α_2 and α_{c2} is approximated to the average values over the temperature interval of interest; (3) the total hole free volume of the system is computed by using the free volume parameters K_{11}/γ_1 and K_{21}/γ_2, which are determined from pure component data for solvent and polymer; (4) the activation energy for the solvent jump, E, depends on the polymer concentration since the energy per mole needed by the solvent molecule to overcome attractive forces depends on its neighbors. The transition from the energy in the concentrated region to the region near the pure solvent limit is assumed to be smooth as ω_1 approaches unity [183].

Eq. (41) can be simplified in the special case of pure solvent or very low polymer concentrations:

$$\log\left(\frac{D}{D_0}\right) = \frac{-\xi V_2\omega_2}{2.303K_{11}(K_{21} - T_{g1} + T)/\gamma} \tag{44}$$

The parameters K_{ij}, γ and T_{gi} are available in the literature for many common organic solvents and polymers [20,179,184,185].

Eqs. (41) and (44), though complicated in their forms, were used successfully to fit experimental data of diffusion. For example, Lodge et al. [186] used the forced Raleigh scattering technique to measure tracer diffusion in poly(vinyl acetate)–toluene system. Agreement between the model of Vrentas and Duda, or Fujita's model, and the experimental data was good over the entire range of polymer concentrations (0–96 wt%). Similar results were published by Zielinski et al. [187] who studied diffusion in PS

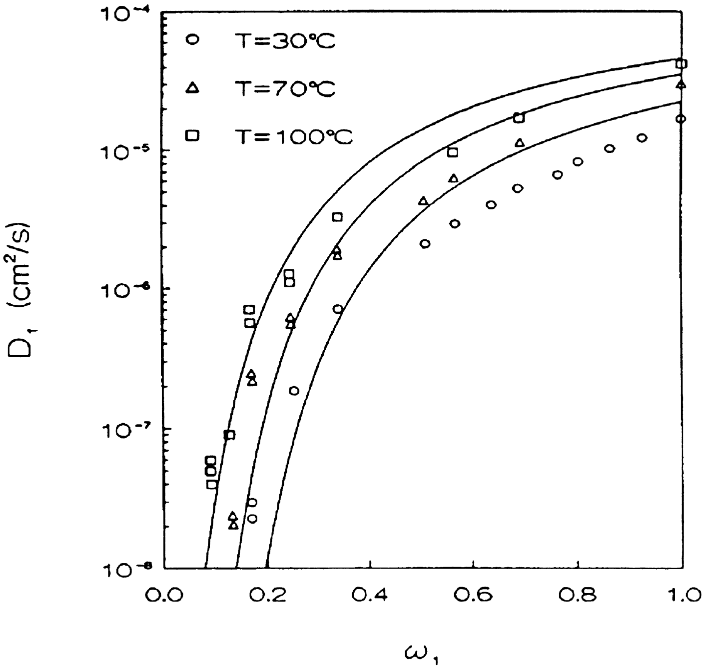

Fig. 9. Semilogarithmic plot of the self-diffusion coefficient of ethylbenzene in polystyrene as a function of the mass fraction of the solvent, at different temperatures. The solid lines are the theoretical predictions of the solvent diffusion using the free volume theory of Vrentas and Duda (Section 2.3.3). Reprinted with permission from AIChE J 1992;38:405. ©1999 American Institute of Chemical Engineers [185].

solutions by static field gradient NMR, and Wisnudel and Torkelson [20] who studied small molecule diffusion in PS by the Taylor dispersion technique. Other studies have also demonstrated good agreement with this model [136,188,189]. However, several papers reported problems that occurred below the glass transition temperature [65,166,184,187]. Correlation with the data was achieved only with negative values for the polymer free volume parameter, which is impossible [65,184,187]. This problem was overcome recently by Vrentas and Vrentas who introduced a specific hole free volume, $\hat{V}^0_{2g}$, of the glassy polymer at any temperature below T_{gm} (glass transition temperature of the polymer–solvent mixture) at a particular temperature [176,184].

Despite the re-examination of the model by Vrentas and Vrentas [183,190] in order to provide a better agreement with diffusion data over a large temperature range and under the glass transition temperature, certain failures have been demonstrated. For example, Waggoner et al. [36] showed that this model cannot fit the data in the low polymer concentration region. Similar conclusions were also made by Hong et al. [191] Wisnudel and Torkelson [20] pointed out that the diffusion model of Vrentas and Duda did not take into account the flexibility of the diffusant, as they noticed poorer agreement with flexible diffusants than with rigid ones. Zielinski and Duda [185] expected that the model of Vrentas and Duda will deviate from experimental observations at high temperatures (150°C above T_g) because the diffusion will be no longer limited by the free volume. Energy effects will become dominant.

Some papers compared the free volume models of Vrentas and Duda with the original free volume theory of Fujita. According to Landry et al. [192], the application of both models had no difference. The same conclusion was drawn by Lodge et. al. [186], but they also concluded that the model of Vrentas and Duda is successful as a predictive theory over the complete range of polymer concentrations, and over a substantial range of temperatures (above the glass transition temperature), whereas Fujita's model cannot be used to predict or examine the temperature dependence.

Zielinski and Duda [185] used the free volume model of Vrentas and Duda to estimate the diffusion of organic solvents in polymer systems. Their work seemed to be among the first attempts in diffusion prediction reported in the literature. First, they reviewed the literature to evaluate the independent parameters necessary to apply the model. Then, they estimated the diffusion of solvents (toluene, ethylbenzene, chloroform, methyl acetate, and tetrahydrofuran) in polymer systems (PS, PVAc, PMA, and PMMA). They obtained fairly good correlations with the experimental data (Fig. 9). Guo et al. [59] tried to predict the diffusion coefficients of benzene, *o*-xylene, ethylbenzene, and chloroform in natural rubber membranes using the approach of Zielinski and Duda [185]. They did not found good agreements and suggested that the parameters proposed by Zielinski and Duda [185] did not yield acceptable predictions of the diffusion coefficients.

An important point to be underlined is that the model of Vrentas and Duda needs numerous parameters. For example, Duda and coworkers [193] mentioned that 14 independent parameters are necessary to apply this model. Among these 14 parameters 10 need to be evaluated in order to predict the self-diffusion coefficient. Furthermore, these parameters are not usually available in the literature for many polymers, especially new ones.

2.3.4. The model of Peppas and Reinhart

For the treatment of transport mechanism in cross-linked polymer networks, Peppas and Lustig [194] considered three different kinds of structures: (1) macroporous hydrogels defined by pore size greater than 0.1 μm where the mechanism of transport is mainly due to convection; (2) microporous hydrogels characterized by pore size in the range of 20–500 Å (diffusants and pores have similar dimensions) where the mechanism of transport is due to both diffusion and convection; (3) nonporous hydrogels for which space between the macromolecular chains is limited and where the mechanism of transport is due to diffusion only [194].

In pharmaceutical applications such as drug releases, nonporous hydrogels seem to be more often used than macroporous or microporous gels [194]. The discussion here is focused on nonporous hydrogels. More information on convection and diffusion in macro- and microporous gels can be found in the paper by Peppas and Lustig [194].

The model of Peppas and Reinhart [195] was also based on the free volume concept [27,171]. Diffusion is said to occur through the gel space not occupied by polymer chains. Thus, the self-diffusion coefficient of a diffusant is considered proportional to the probability of moving through the gel with mesh size, P_ξ, but also proportional to the probability of finding the required free volume in the gel and solution, P'_0/P^+_0, which is given by the following equation:

$$\frac{D}{D_0} = P_\xi \frac{P'_0}{P^+_0} \tag{45}$$

where D is the solute diffusion coefficient in the hydrogel, D_0 is the solute diffusion coefficient in water.

The probability, P'_0/P^+_0, of finding the required free volume was analyzed by Peppas and Reinhart [195]. They also assumed that the free volume available for the solute diffusion was mainly due to water,

Table 6
Summary of the diffusion models based on the free volume theories (Section 2.3)

Author(s)	Reference(s)	Application(s)	Limitation(s)
Fujita	[27]	Solvents and small-sized diffusants Semi-dilute polymer solutions	Large diffusants Concentrated polymer solutions
Yasuda et al.	[171]	Solvents and small-sized diffusants Semi-dilute polymer solutions	Large diffusants Concentrated polymer solutions
Vrentas and Duda	[175–178]	Various solutes and solvents	Determination of the numerous parameters
		Both semi-dilute and concentrated polymer solutions	Dilute polymer solutions
Peppas and Reinhart	[195]	Various solutes and solvents	Diffusants with size closer to or greater than the mesh size of the network
		Chemically cross-linked gels and hydrogels	Diffusion in non-cross-linked polymers

and little from the polymer. The following expression was then obtained [195].

$$\frac{D}{D_0} = P_\xi \exp\left(-\frac{Y}{Q-1}\right) \tag{46}$$

where $Y = k_2 R_\mathrm{h}^2$, and Y is a structural parameter near unity and proportional to R_h^2, k_2 a parameter of the polymer–water system, R_h the solute hydrodynamic radius, and Q the volume degree of swelling for the gel.

The probability, P_ξ, of moving through the mesh size, ξ, was studied later by Reinhart and Peppas [196] who demonstrated that this quantity is related to a critical mesh size, M_c^*, below which the diffusion of a solute of size R_h could not occur:

$$P_\xi = \frac{M_\mathrm{c} - M_\mathrm{c}^*}{M_\mathrm{n} - M_\mathrm{c}^*} \tag{47}$$

where M_c is the number average molecular weight between cross-links, M_n the number average molecular weight of uncross-linked polymer. In fact, M_c^* represents the minimal distance in monomer unit between two cross-link points for which diffusion is possible.

Combining Eqs. (46) and (47), the diffusion coefficient in highly swollen membranes can be expressed by

$$\frac{D}{D_0} = k_1 \frac{M_\mathrm{c} - M_\mathrm{c}^*}{M_n - M_\mathrm{c}^*} \exp\left(-\frac{k_2 R_\mathrm{h}^2}{Q-1}\right) \tag{48}$$

where k_1 is a structural parameter of the polymer–water system.

To describe solute transport in moderately swollen networks [197], they considered that in a moderately swollen network the free volume was not equal to the free volume of the solvent, and that diffusion jump length of the solute in solution was not equal to that of the solute in water. A new equation was derived:

$$\frac{D}{D_0} = \frac{\lambda^2}{\lambda_0^2} B(\nu^*) \exp\left[-\nu_s \left(\frac{1}{V} - \frac{1}{V_0'} \right) \right] \tag{49}$$

where λ^2 and λ_0^2 are the diffusion jump lengths of the solute in the hydrogel and water, respectively, $B(\nu^*)$ is a term representing the characteristic size of the space available for diffusion in the membrane, ν_s is the size of the diffusing solute, and V and V_0' are the free volumes in the swollen membrane and water, respectively [198].

Peppas and coworkers have published several papers with diffusants of various sizes in various hydrogels which showed agreement with the model [198–202]. Recently, they have also pointed out the limitations of this model. For example, Peppas and coworkers [202,203] studied the diffusion of ionized diffusants in charged hydrogels and found that they were much more hindered than the larger proteins because of their interactions with ionized carboxylic acid groups [203]. Thus, a parameter relating the interactions between ionized diffusants and the network should be introduced. In addition, problems may also occur when the diffusant size is close to or larger than the mesh size in the network due to screening effects.

2.3.5. Summary

The free volume models have found various success in the description of diffusion in polymer systems. The advantages and constraints for each model described in this section are summarized in Table 6. The model of Vrentas and Duda [175,176] seems to be the most useful as it is applicable over a large range of polymer concentrations and temperatures. However, obtaining the numerous parameters required represent quite a task since these parameters are not always available in the literature. When these parameters are known, it is possible to predict solvent diffusion in certain binary systems.

The model of Peppas and Reinhart [195] describes specifically diffusion in cross-linked gels. Problems may arise when the size of the diffusant is close to or larger than the network mesh size, and when the diffusant is bound to the polymer network by ionic interactions. It does not seem to be applicable to describe diffusion in polymer solutions where there is no cross-linking.

Manz and Callaghan [147], and Xia and Wang [167] also suggested the use of William–Landel–Ferry [204] (WLF) equation and Vogel–Fulcher–Tammann [167] (VFT) equation for the interpretation of diffusion data, but they cannot be used below T_g [147,167].

2.4. Other physical models of diffusion

Many of the diffusion models did not offer temperature dependence since most experiments were carried out at room temperature. Variable temperature diffusion data can be analyzed with physical models that can be considered as thermodynamic models. We also include here other models that do not fit to the descriptions in the previous categories.

2.4.1. Arrhenius' theory

Arrhenius equation describes the temperature dependence of a chemical reaction rate as illustrated by

Table 7
Example of activation energy (E_a) studies based on Arrhenius equation found in the literature (Section 2.4.1). *o*-MR and *p*-MR stand for *ortho*- and *para*-methyl red, respectively

	System	E_a (kJ/mol)
Sung and Chang [51]	*o*-MR in toluene	11.9
Temperature: 15–55°C	*p*-MR in toluene	12.6
Polymer concentration	*o*-MR in toluene/PS	13.6
(PS and PVAc): 10 wt%	*p*-MR in toluene/PS	15.1
	o-MR in toluene/PVAc	17.2
	p-MR in toluene/PVAc	21.7
Gao and Fagerness [32]	H_2O + 0.5% adinazolam	
Temperature: 10–50°C	+2% glusose, or lactose, or HPMC	
	– Water diffusion	4.3–4.6
	– Adinazolam diffusion	5.0–5.3
Nyström et al. [69]	Cellulose/H_2O	23.3
Temperature: 14–44°C	Cellulose/H_2O/D_2O	17.0
Concentration: $\varphi_p = 0.093$	Cellulose/H_2O/D_2O/Dioxane	15.0
	Cellulose/H_2O/D_2O/*t*-Butanol	24.1
Pickup and Blum [65]	Toluene in PS	11–68
Temperature: 25–115°C		
Concentration: $\varphi_p = 0.04$–0.90		

[205]

$$k = A\exp\left(-\frac{E_a}{RT}\right) \tag{50}$$

where k represents the kinetic rate of a chemical reaction, A a pre-exponential factor and E_a the activation energy. Eq. (50) can be written in a logarithmic form

$$\log k = \log A - \frac{E_a}{RT} \tag{51}$$

which is useful to estimate E_a from a plot of logarithmic k versus $1/T$.

Some recent works reported diffusion experiments at different temperatures which led to the evaluation of the activation energy of diffusants in polymer systems with the Arrhenius equation [32,65,69].

$$D = A\exp\left(-\frac{E_a}{RT}\right). \tag{52}$$

Examples of E_a values found in the literature are given in Table 7. From the activation energy of a diffusant in a given system, we can obtain information of the network in which the diffusion takes place. In order to obtain complementary information, it is necessary to compare the E_a values in different systems for the same diffusant. However, the Arrhenius equation does not provide any correlation to the diffusant size or to the polymer networks. In addition, Arrhenius model seems valid only in dilute systems because *the diffusion rate is limited by the energy required for the diffusing species to escape*

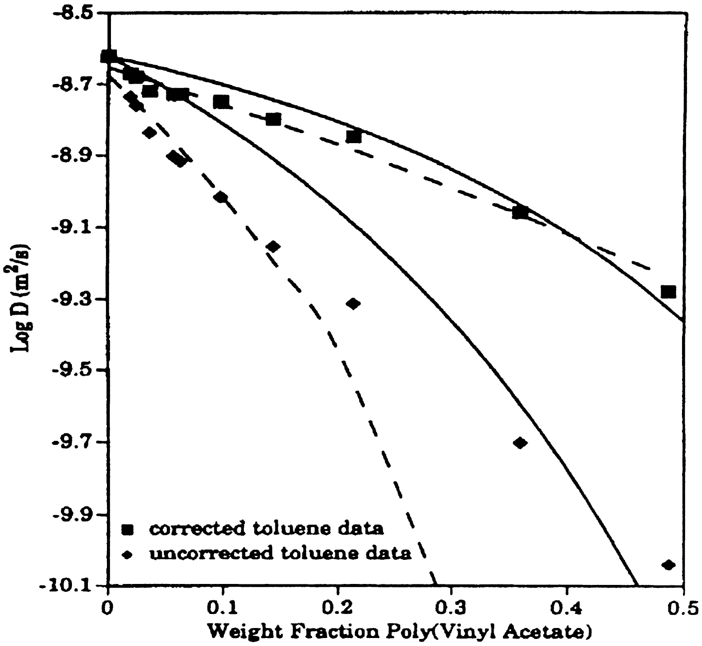

Fig. 10. The self-diffusion coefficients of methyl red plotted as a function of PVAc concentration in toluene. Data displaying the hydrogen-bonding effect (diamonds) and data with the hydrogen-bonding effect removed (squares) are fitted with the free volume model of Vrentas and Duda (solid lines), Eq. (41), and the modified Enskog theory (dotted lines), Eq. (53). Reprinted with permission from Macromolecules 1993;26:6841. ©1999 American Chemical Society [36].

its present surroundings and move into an adjacent environment. However, in moderate to high concentration solutions, the diffusion process is limited by the polymer molecular motions [36].

2.4.2. The modified Enskog theory

The modified Enskog theory was recognized to provide a suitable description of gas and liquid diffusion in membranes [206]. As shown by Waggonner et al. [36], this model can also be employed to describe the diffusion of a diffusant in polymer networks. The diffusant particle was represented as a rigid sphere flowing through the polymer solution. The diffusion coefficient of such a tracer particle is given by

$$D_\alpha = \frac{1}{\dfrac{1}{D_{\alpha \mathrm{M}}} + \dfrac{1}{D_{\alpha\beta}}\left[1 - x_\alpha\left(1 - \dfrac{D_{\beta \mathrm{M}}}{D_{\alpha \mathrm{M}}}\right)\right]} \tag{53}$$

where D_α represents the self-diffusion coefficient of the tracer, α, β and M represent the tracer, the solvent and the polymer, repectively, D_{ij} the mutual diffusion coefficient of component i with respect to component j and x_α is the molar fraction of the tracer. Consequently, $D_{\alpha \mathrm{M}}$ is the mutual diffusion coefficient of the tracer with respect to the polymer, $D_{\alpha\beta}$ the mutual diffusion coefficient of the tracer with respect to the solvent, and $D_{\beta \mathrm{M}}$ the mutual diffusion coefficient of the solvent with respect to the polymer.

Further, if the tracer molecule is present in a small quantity and if both tracer and solvent have

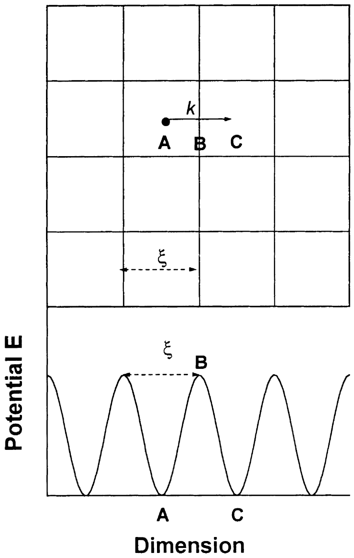

Fig. 11. Representation of the polymer solution of a network of mesh size ξ and potential E for the diffusion process of a diffusant in a polymer network. Reprinted with permission from Macromolecules 1996;29:6031. ©1999 American Chemical Society [33].

approximately the same mutual diffusion coefficient with respect to the polymer, Eq. (53) can be rewritten as

$$\frac{1}{D_\alpha} = \frac{1}{D_{\alpha \mathrm{M}}} + \frac{1}{D_{\alpha\beta}}. \tag{54}$$

This equation offers a simple dependence on the tracer diffusion coefficient in a dilute solution. The respective mutual diffusion coefficient, $D_{\alpha\beta}$, can be expressed as [206]

$$D_{\alpha\beta} = \frac{3}{8n\sigma_{\alpha\beta}^2}\left(\frac{\mathrm{k}T(m_\alpha + m_\beta)}{2\pi m_\alpha m_\beta}\right)^{1/2}\frac{1}{g_{\alpha\beta}(\sigma_{\alpha\beta})} \tag{55}$$

where n is the number of molecules per unit volume or the number density (mol/cm^3), $\sigma_{\alpha\beta}$ the hard sphere collision diameter of component α and β, m_i the molecular mass of component i, and $g_{\alpha\beta}(\sigma_{\alpha\beta})$ is the rigid sphere contact radial distribution function. This function was obtained from the scaled particle theory and depends on the molecular radius of the component and on the molecular friction coefficient [206].

The modified Enskog theory was mainly employed for gas diffusion through membranes and not often used for polymer solutions. However, Waggoner et al. [36] used this model to draw up comparisons between the modified Enskog theory, the model of Vrentas and Duda and the model of Mackie and Meares in various polymer systems (PS and PMMA). They concluded that Enskog's model provided satisfactory correlation with the experimental data at lower polymer concentrations exclusively. At higher polymer concentrations the authors observed little correlation between theoretical predictions and experimental results (Fig. 10). This conclusion is consistent with the work of Pickup and Blum [65].

It should be noted that the modified Enskog theory does not provide a polymer concentration dependence.

2.4.3. The model of Petit et al.

Petit et al. [33] proposed a new physical model for the diffusion of solvents and solute molecules in polymer solutions and gels. This model considered the medium as a transient statistical networks of an average mesh size ξ, as defined by de Gennes [123], in which the diffusing molecules have to overcome energy barriers of equal magnitude (Fig. 11). The transient network is considered to exist over the whole range of polymer concentrations including the dilute regime. A diffusing molecule is considered as residing temporarily in a cavity and diffusion occurs only when the particle has enough energy to jump over an energy barrier to move forward to the next cavity. Thus, diffusion is considered as a succession of jumps over energy barriers. Petit et al. [33] considered one-dimensional diffusion assuming that the energy potentials are equal in amplitude, ΔE, and spaced by equal intervals ξ, which corresponds to the correlation length. Introducing k as the solute jump frequency, Fick's first law of diffusion can be written as follows, according to Andreoli et al. [207]

$$D = \xi^2 k \tag{56}$$

where k, the jump frequency, is expected to depend on both temperature and size of the diffusant. The jump frequency can be written in an Arrhenius form, according to Kramer [208] who studied the jump of Brownian particles over one potential barrier,

$$k = F_{\mathrm{P}} \exp\left(-\frac{\Delta E}{\mathrm{k_B} T}\right) \tag{57}$$

where F_{P} is a frequency pre-factor, ΔE the height of the potential barrier, $\mathrm{k_B}$ is the Boltzmann constant and T the temperature. Furthermore, dependence of ξ on the concentration was given by de Gennes' relation [122]:

$$\xi = R_{\mathrm{g}}\left(\frac{c^*}{c}\right)^{\nu} = \beta c^{-\nu} \tag{58}$$

where R_{g} is the radius of gyration of the polymer, c^* the overlap concentration between the dilute and semi-dilute regimes, c the polymer concentration and ν is a parameter. In de Gennes' theory, ξ was said to depend on the polymer concentration but not on the molecular weight of the polymer when $c > c^*$ [123]. Substituting Eq. (58) into Eq. (56) leads to the following equation:

$$D = k\beta^2 c^{-2\nu}. \tag{59}$$

This equation is not suitable to describe the diffusion of a diffusant at zero polymer concentration. Therefore Petit et al. [33] considered the friction coefficients of the diffusing molecules to formulate a better expression. It is generally assumed that the total friction coefficient, f, experienced by a diffusing molecule in a polymer solution results from an additive contribution of the background solvent, f_0, and the polymer network, f_{p} [209,210]

$$f = f_0 + f_{\mathrm{P}}. \tag{60}$$

By the use of Stokes–Einstein relation, $D = \mathrm{k_B}T/f$, and by the use of Eq. (59), Eq. (60) can be

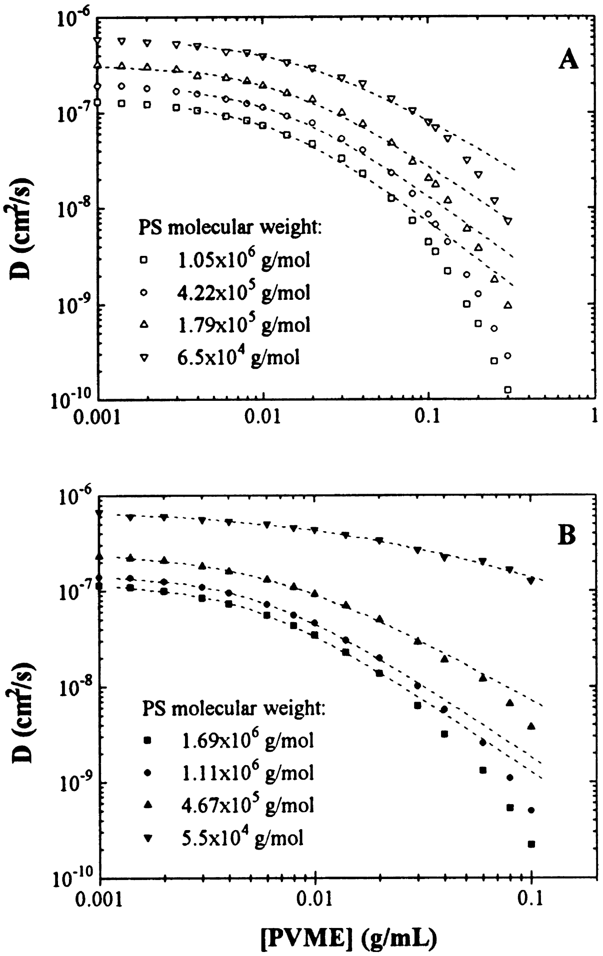

Fig. 12. The logarithmic plots of the self-diffusion coefficients of (a) a linear PS and (b) a 12-arm star PS in PVME/*o*-fluorotoluene as a function of the PVME concentration, at 30°C (data from the work of Lodge and coworkers [45,111]). Dashed lines are fittings to Eq. (62).

rewritten as

$$\frac{1}{D} = \frac{1}{D_0} + \frac{1}{k\beta^2 c^{-2\nu}} \tag{61}$$

where D_0 is the diffusion coefficient of the diffusant in the absence of the polymer. Eq. (61) can be rewritten as

$$\frac{D}{D_0} = \frac{1}{1 + ac^{2\nu}} \tag{62}$$

where D_0 is the diffusion coefficient of the diffusant in absence of the polymer, $a = D_0/k\beta^2$ and ν is a characteristic parameter of the system that can be regarded as a constant. The value of k is not constant because F_P and ΔE (Eq. (57)) should both depend on the polymer concentration. Nevertheless, k can be approximated as a constant within a certain range of concentrations, although k may have a certain dependence on the mesh size of the network. The parameter β is expected to be constant for a given system so that $k\beta^2$ depends only on the solute size and on the temperature.

The model of Petit et al. [33] was employed to analyze the diffusion data of both solute molecules in ternary aqueous polymer (PVA) systems and solvents (esters and ketones) in binary polymer (PMMA) organic solutions over a wide range of concentrations [211,212]. It has successfully described the effect of polymer concentration and temperature dependence. Recently, this model was used to treat the diffusion data of both small and large diffusants varying from ethylene glycol ($M = 62$ g/mol) up to poly(ethylene glycol) with a molecular weight of 4000 [211]. This diffusion model provided good agreements with the experimental data. In addition, it was used to analyze variable temperature of diffusants of various sizes. The activation energy calculated was found to increase with increasing size of the diffusant. Furthermore, an empirical relationship was found between the parameter $k\beta^2$ and the hydrodynamic radius of the linear PEG diffusants

$$\log k\beta^2 = -0.0356R_h - 10.45. \tag{63}$$

In order to further test the validity of this model, diffusion data can be gathered from the literature. For example, Wheeler and Lodge [45] studied the self-diffusion of linear PS ($M = 6.5 \times 10^4, 1.79 \times 10^5, 4.22 \times 10^5,$ and 1.05×10^6) in *o*-fluorotoluene solutions of PVME ($M = 1.4 \times 10^5, 6.3 \times 10^5$, and 1.3×10^6), with concentrations ranging from 0 to 0.30 g/ml. In a companion paper, Lodge et al. [111] studied the self-diffusion of 3-arm ($M = 6.5 \times 10^4, 1.79 \times 10^5, 4.22 \times 10^5,$ and 1.05×10^6) and 12-arm ($M = 6.5 \times 10^4, 1.79 \times 10^5, 4.22 \times 10^5,$ and 1.05×10^6) star polystyrenes in the same system. These diffusion data were analyzed with the model of Petit et al. [33], and the results are shown in Fig. 12 for the linear and 12-arm star PS diffusants, respectively. It seems that the model of Petit et al. [33] is not accurate to describe diffusion of linear and star diffusant with molecular weight similar to the background polymer, in this organic solvent, despite its success with macromolecular diffusants in polymer gels [211,212].

2.4.4. Amsden's model

Recently, Amsden [28] published a brief review of several diffusion models including the models proposed by Yasuda et al. [171], Ogston et al. [76], Johansson et al. [31], Altenberger et al. [97], Cukier [26], and Phillips [213]. The combined obstruction and hydrodynamic theories proposed by Brady [214] was also discussed in the review. In the author's opinion, the obstruction and hydrodynamic models cannot adequately describe the diffusion behavior of macromolecules within stiff-chained hydrogels, and the combined obstruction and hydrodynamic theories can provide a better approximation of the diffusion data but do not predict the effect of solute radius on its reduced diffusivity. Therefore, Amsden [28] proposed a new diffusion model which is based on the equation of Lustig and Peppas [199]. According to Amsden [28], the transport of a molecule through the hydrogel is proportional to the probability of finding a succession of holes larger than the diffusant diameter. Therefore, the effective diffusivity of the diffusant, $\bar{D}_e$, is expressed as

$$\bar{D}_e = \bar{D}_m \int_{r^*}^{\infty} g(r)\,dr \tag{64}$$

where $\bar{D}_{\mathrm{m}}$ is the average mutual diffusion coefficient of the solute, $g(r)$ the distribution of spheres within the hydrogel, and r^* the critical sphere radius required for solute diffusion.

In the case of straight polymer fibers randomly dispersed in the hydrogel network, the distribution of spheres $g(r)$ can be expressed as

$$g(r) = \frac{\pi r}{2R^2}\exp\left[-\frac{\pi}{4}\left(\frac{r}{R}\right)^2\right] \tag{65}$$

where R is the mean radius of the distribution.

Substituting Eq. (65) into Eq. (64) and carrying out the integration, one can obtain

$$\frac{\bar{D}_e}{\bar{D}_m} = \exp\left[-\frac{\pi}{4}\left(\frac{r^*}{R}\right)^2\right]. \tag{66}$$

To account for the specific polymer thickness, Amsden rewrote Eq. (66) to include the average radius of space between the polymer chains, $\bar{r}$, and the radius of the polymer chain, r_{f}:

$$\frac{\bar{D}_{\mathrm{e}}}{\bar{D}_{\mathrm{m}}} = \exp\left[-\frac{\pi}{4}\left(\frac{r_{\mathrm{s}}+r_{\mathrm{f}}}{\bar{r}+r_{\mathrm{f}}}\right)^2\right]. \tag{67}$$

$\bar{r}$ can be approximated as the average end-to-end distance between the polymer chains, ξ. Further, from scaling concepts ξ was found dependent on the polymer volume fraction

$$\xi = k\varphi^{-1/2} = k_1 r_{\mathrm{f}}\varphi^{-1/2} \tag{68}$$

where k is a constant for a given polymer–solvent system, dependent on the length of the monomer unit and the stiffness or flexibility of the polymer chain. k can be expressed as a function of the polymer chain radius, $k = k_1 r_{\mathrm{f}}$. Substitution of Eq. (68) into Eq. (67) leads to the final form of Amsden's diffusion model [28]

$$\frac{\bar{D}_{\mathrm{e}}}{\bar{D}_{\mathrm{m}}} = \exp\left[-\pi\left(\frac{r_{\mathrm{s}}+r_{\mathrm{f}}}{r_{\mathrm{f}}}\right)^2\frac{\varphi}{(k_1+2\varphi^{1/2})^2}\right] \tag{69}$$

Thus, this model takes into account the polymer structural properties such as the polymer chain stiffness, the polymer chain radius, the polymer volume fraction as well as the size of the diffusant. According to Amsden, the model predicts a decrease of the solute diffusion when the polymer volume fraction increases, when the diffusant size increases, and when the radius of the polymer chain decreases [28].

Eq. (69) was tested by studying protein (pepsin, ovalbumin, BSA and β-lactoglobulin) release from calcium alginate matrices. Amsden found that Eq. (69) provided a good correlation with the experimental data over the entire range of polymer volume fractions investigated ($\varphi = 0$–0.05) [28]. The dependence of the diffusion on the hydrodynamic radius of the solute was also predicted properly. Amsden [28] also tried the simulation of the data published by Johansson et al. [31,77], which demonstrated that the model was capable of describing the effect of polymer chain radius and flexibility on the diffusion of solutes.

2.4.5. Summary

The theories presented in Sections 2.4.1 and 2.4.2 were not intended to describe diffusion in polymer solutions and gels, but they are useful in the description of the diffusion behavior, particularly the temperature effect. Other thermodynamic models such as Eyring' model [215] were not discussed here because of the limitations in their applicability.

The model of Petit et al. [33] describes the dependence of diffusion on the molecular size of the diffusant, polymer concentration as well as temperature. This model was used successfully to link the diffusion of small and macromolecules in binary and ternary polymer systems. Nevertheless, the examination of certain diffusion data from the literature showed its limitations for the diffusants of high molecular weights in concentrated polymer networks.

The new diffusion model defined by Amsden [28] combined the obstruction effect and the hydrodynamic interactions and seemed an interesting approach. Further tests with more concentrated polymer networks need to be done to verify its usefulness.

3. Concluding remarks

Diffusion in polymer systems is a complicated process. It depends on the properties of the diffusants, the polymer network, and the solvents. The obstruction by the polymer network, the hydrodynamic interactions in the system, and the thermodynamic agitation should be all considered to understand the diffusion in polymer solutions, gels and even solids. Various models and theories succeeded in describing the diffusion process under different circumstances, and all contributed to the understanding of diffusion phenomena. Enormous progress has been made in the field but controversies are not uncommon. It seems also fair to say that limitations exist for the application of the physical models and care should be taken in the use of the models for the interpretation of the results obtained. It remains difficult, if not impossible, to estimate and predict the diffusion coefficient of a given diffusant in a given system under specific conditions. It is also important to establish a correlation between the self-diffusion behavior in an equilibrated state and the diffusion in a real time non-equilibrated dynamic situations, where the swelling and the dissolution of the polymer matrix, the compatibility of the solvent, solute and polymer should all be considered.

The rapid development of various techniques such as NMR allows the study of more complicated systems to obtain further information on the properties of the diffusants and polymeric networks. For example, it is now possible to track the release of solutes such as drugs from a polymer matrix in real-time situations by NMR imaging [216]. Studies of this kind should generate more results, leading to a better understanding of the diffusion process in polymer systems.

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