Transport of Glucose and Poly(ethylene glycol)s in Agarose Gels Studied by the Refractive Index Method

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ABSTRACT: The diffusion of glucose and a series of poly(ethylene glycol)s (PEG, average molecular weight = 200, 600, 1000, 10000) in agarose gels (in the range of 0.5−3%, w/w) have been studied with a novel refractive index method developed in our laboratory. The change of the gel refractive index caused by the change of the diffusing solute concentration in the gel during the diffusion process enables the effective solute diffusion coefficients to be computed. The change in glucose concentration in agarose gel with the diffusion distance and the diffusion kinetics of glucose in agarose gels reveal that glucose diffuses freely within these gel matrixes with a high diffusion coefficient $\sim 6 \times 10^{-10}$ m^2/s for 0.5% and 1.5% agarose gels. However, the diffusion coefficients of PEGs in the gel are generally in the range of $(0.7-5.9) \times 10^{-10}$ m^2/s and decrease with an increase in the network density (higher agarose gel concentration) and/or in the molecular weight of the diffusing solutes. It is observed that the molecular weight dependence of the PEG diffusion coefficients can be described with a power law expression with an exponent −0.533, indicating that PEG in agarose gel is in a situation close to the negligible solvent drainage coil (exhibited in dilute solution with a characteristic exponent −0.5). Furthermore, two models of both Ogston's model and Amsden's model based on the obstruction effect were used to simulate the effect of polymer volume fraction on the diffusion coefficients of the solutes in agarose gel to account for the results.

Introduction

Molecular diffusion in porous media such as hydrogels is not only closely related to bioseparation method but also crucial for deeply understanding the transport processes of small molecular or macromolecular drugs and natural macromolecules in organisms.[1−3] For example, the present most advanced technique for curing cancer in medical science is "close therapeutics", where the drug is dissolved in the pregel solution, and then the mixture is injected into the site where the focus stays. The pregel solution gels and then adheres to the surface of the focus to realize a site-specific close therapeutics. During this process, there is a diffusion process of the drug molecules from the gel toward the focus. Therefore, research in interactions between drug molecules and hydrogel network has a great scientific value toward the development of medical science. Agarose is a polysaccharide with a main chain consisting of 1,3-linked D-galactopyranose and 1,4-linked 3,6-anhydro-R-L-galactopyranose.[4] In recent years, the structure and properties of agarose gels have been characterized because of their importance in gel chromatography, but a full understanding is still lacking.[5] Research results have revealed that agarose gels have typical characteristics that resemble the living tissues in composition, rheological nature, and water content and therefore have been widely used as artificial tissues to study small molecules or macromolecules transportation process, which could be expected to closely simulate in vivo molecular transport in living tissues.[6]

Glucose is a small neutral biomolecule widely used in medical treatment. For several years, great efforts have been made in seeking for effective techniques for in situ monitoring the physiological glucose levels to improve quality of life for diabetic patients. The ability to obtain information without breach of the skin would certainly improve patient comfort and compliance.[7] Furthermore, monitoring glucose level remotely and continuously will contribute a lot to the design or development of new precepts for curing this kind of obstinate disease. Poly(ethylene glycol) (PEG) is unbranched highly flexible polymer, which is unique in that they are soluble in both organic and aqueous solvents. Water is a good solvent for PEG, ensuring easier prediction of the properties in water than in nonideal systems.[8] Furthermore, PEGs are easily available commercially in a series of molecular weights with a polydispersity factor close to 1, which avoids the trouble in accounting the influence of polydispersity on the solution behavior of PEGs.

Over the past several decades, a number of methods have been applied or established to investigate the diffusion behavior of small molecules or macromolecules in hydrogels, such as light scattering,[5] nuclear magnetic resonance microscopy (NMR),[1,9] fluorescence spectroscopy,[10,11] Fourier transform infrared microscopy (FT-IR),[12,13] and electrochemical techniques.[14,15] The conventional method for studying the diffusion behavior in hydrogel matrices is usually by measuring the change of the diffusing solute concentration outside the polymer hydrogel, which is called the intermittent method. In-situ measurements reveal much better accuracy than intermittent methods. Optic methods are moreover advantageous for in-situ monitoring because of their nondestructive characteristics. Osada et al.[16−18] established a kind of optic method, namely, the electronic

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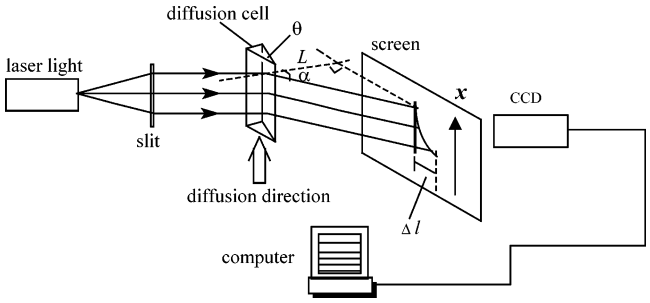

Figure 1. Schematic picture of the in situ refractive index method for measuring the diffusion process.

speckle pattern interferometry (ESPI) based on the interference of light, and applied it to study the diffusion behavior of protein in agarose gel. In our previous work,[19] we introduced a novel optic method, the refractive index method based on a triangular cell, for investigating the diffusion in hydrogels. The method has several obvious advantages over other techniques because of its combining in-situ monitoring and simple technique and thus has been proved to be powerful and promising for studying the molecular diffusion in gels.

In this study, the diffusion behaviors of glucose and PEGs in agarose gels are determined using the refractive index method, mainly concerning the respective role of solute and gel network on the diffusion behavior of the solutes. The significance of this work is that the results will enable a deep understanding of the diffusion behavior of these solutes in a biomimic gel system, which is needed for further progress in research of molecular diffusion in vivo.

Theoretical Background

It is well-known that light will be refracted when passing through a prism, and the refractive angle is closely related to the refractive index of the media in the prism. As shown in Figure 1, when the diffusion solution diffuses from down to up into the hydrogel contained in the triangular cell, the refractive index of the hydrogel changes, leading to the shift of the emergence light. If the shift of the emergence light can be recorded, the change in the refractive index of hydrogel ($\Delta n(t)$) in the cell is represented by[20]

$$\Delta n(t) = \frac{\Delta l(t)\cos\alpha}{L\sin\theta} = \frac{\sqrt{1 - n_0^2\sin^2\theta}}{L\sin\theta}\Delta l(t) \qquad (1)$$

Here $\Delta l(t)$ is the change in the distance between the light strip on the screen and the intersection point of the emergence normal and the screen at time t, L the distance between the emergence point and the screen, and n_0 the initial refractive index of the medium in the cell. θ and α are the incidence angle and refracted angle, respectively.

In terms of the diffusion process that takes place in the triangular cell, the concentration gradient of the diffusing solutes changes as a function of time. The concentration distribution of the diffusing solute in the hydrogels can be determined from the refractive index change of the hydrogels as follows:[16]

$$c(x,t_1) - c(x,t_2) = k[n(x,t_1) - n(x,t_2)] \qquad (2)$$

Here $c(x,t_1)$ and $c(x,t_2)$ are respectively the concentration of the solutes in the hydrogel in the diffusion distance x at time t_1 and t_2. k is a constant. The diffusion process is considered to be controlled by Fick's second law. When the initial and boundary conditions are chosen as $t = 0$, $0 < x < l$, $c = 0$; $x = 0$, $c = C_0$; $t > 0$, $x = 0$, $\partial c/\partial x = 0$, the relationship between concentration profiles of the diffusing solutes and the diffusion coefficients is given by the following equation:[21]

$$\frac{c(x,t)}{C_0} = 1 - \frac{4}{\pi}\sum_{n=0}^{\infty}\frac{(-1)^n}{2n+1}\exp[-D(2n+1)^2\pi^2 t/4l^2] \times \cos\left[\frac{(2n+1)\pi x}{2l}\right] \qquad (3)$$

where l is the length of the gel, D is the diffusion coefficient, and $\partial c/\partial x$ is the concentration gradient along the diffusion direction x axis, as shown in Figure 1. $c(x,t)$ is the concentration of the diffusing solute in the gel at distance x at time t.

Experimental Section

Materials. Agarose was purchased from Donghai Pharmacy Co., Ltd. (Shanghai, China) and used without further purification. PEG of chemical pure, with different average molecular weights (M_w = 200, 600, 1000, 10000) and very low polydispersity index, and glucose of analytically pure were provided by Yili Chemical Reagent Co., Ltd. (Beijing, China). Distilled deionized water was used as solvent.

Preparation of the Agarose Hydrogel. Agarose gels with different agarose concentrations of 0.5%, 1.0%, 1.5%, 2.0%, and 3.0% (w/w) were prepared as follows: The desired weight of dry agarose powder was added to distilled water, and then the mixture was heated to the boiling temperature of the solution for complete dissolution of the agarose. After that, the resulting agarose solutions with various concentrations were poured into a special triangular diffusion cell to form gels upon slowly cooling to room temperature. Before the agarose solution gelled, a suitable triangular rubber block of 6 mm thickness was inserted into the cell to keep the surface of the gel in the cell flat. The surface of the rubber was even to the upside of the cell. When the cell was dipped into the diffusion solution on the headstand, the rubber was pulled out under the solution surface. In this way, the interface between the gel and the diffusion solution was set higher than the outside solution surface to permit the laser beam pass through the position close to the interface between the gel and the diffusion solution. The volume fraction (φ) of agarose in the gel was calculated with a density of dry agarose powder (1.64 g/mL[22]) and a mass fraction of agarose in the agarose gel fiber (0.625)[23] according to Pluen's method.[22] The refractive indexes of the gels (n_0) were measured according to the method described in our previous work.[20] The 100 g/L glucose solution was prepared by dissolving the glucose powder of desired amount in distilled water. A 50 g/L PEG solution was prepared by adding the desired amount of PEG into distilled water.

Measurements and Analysis of Diffusion Coefficients. The diffusion coefficients of glucose and PEGs were measured by the newly developed refractive index method. The principle of the experiment was elucidated in the previous paper.[19] A He−Ne laser (λ = 632.8 nm) was used as the light source. A parallel laser beam passed through the triangular gel cell and formed a linear light strip on the screen. During the diffusion process, the linear light strip will bend to one side because the refractive index of the gel system changes in the presence of the solutes. The triangular cell with one acute angle of 30° was made with spectralite. The diffusion process of the drug was generally performed at 25 ± 0.5 °C. After the cell with gel inside was dipped into the diffusion solution in a container where a small magnetic stirrer was placed to keep the diffusion solution homogeneous, the change of the light strip of the emerging light was recorded in situ with a CCD camera (JT-

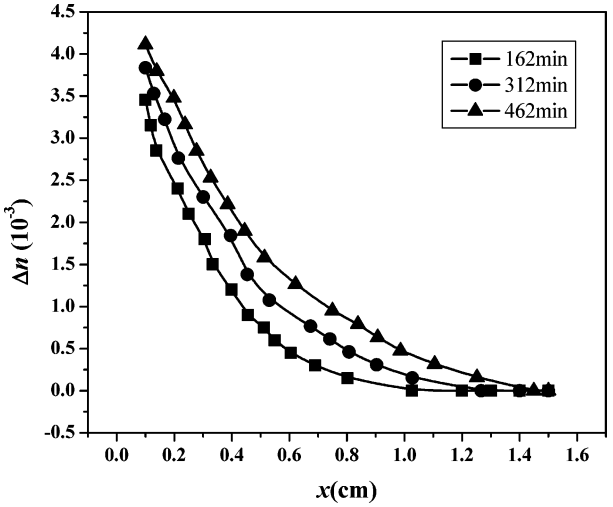

Figure 2. Dependence of the refractive index change on the diffusion distance for the diffusion of 100 g/L glucose in 1.5% agarose gel at 25 °C after 162, 312, and 462 min.

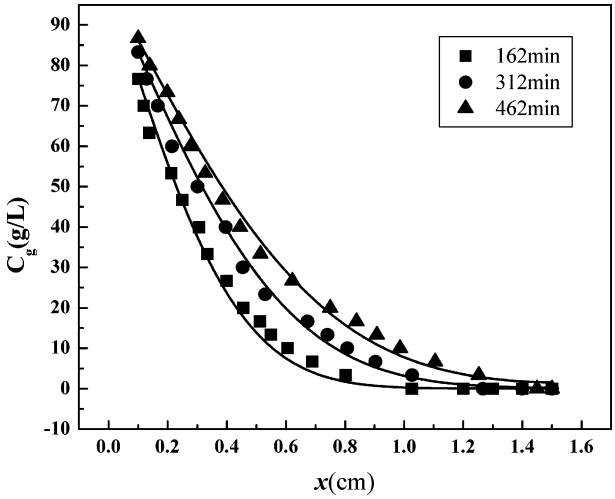

Figure 3. Distribution of the solute concentration as a function of the diffusion distance for 100 g/L glucose in 1.5% agarose gel at 25 °C after 162, 312, and 462 min. The lines are calculated from Fick's second law, assuming a glucose diffusion coefficient of 5.73×10^{-10} m^2/s.

2172, Japan). The measurement begins within 3 min after the solution was introduced into the diffusion cell. Images of the light strip were saved on a hard disk and treated with a specific program via computer. The reproducibility of experimental data was assessed by running each experiment in triplicate and averaging.

Results and Discussion

Diffusion of Glucose in Agarose Gel. The solutes distribution within hydrogels and the diffusion coefficients have been evaluated successfully through our established nondestructive refractive index method. Figure 2 shows the evolution of the refractive index change of a 1.5% agarose gel as a function of the diffusion distance in the presence of 100 g/L glucose aqueous solution as the diffusion solution after 162, 312, and 462 min of diffusion. The change of refractive index denotes the ingress of glucose into the agarose gel. The refractive index change decreases exponentially with an increase in the diffusion distance, indicating that a large concentration gradient of glucose exists in the agarose gel during the diffusion process. The penetration distance, namely, the position where the refractive index of the gel system start to change, increases from 1.02 to 1.44 cm when the diffusion time increases from 162 to 462 min. Furthermore, the refractive index change are 3.45×10^{-3}, 3.83×10^{-3}, and 4.11×10^{-3} for diffusion time 162, 312, and 462 min, respectively, showing that this refractive index method can in-situ trace the whole diffusion process of glucose under nondestructive circumstances.

According to eq 2, the refractive index change of the agarose gel during the diffusion process can be converted to the change of glucose concentration in agarose gel, as shown in Figure 3. The glucose concentration of the glucose at the diffusion distance 0.1 cm increases from 76 to 86 g/L with an increase in the diffusion time from 162 to 462 min, indicating the occurrence of glucose diffusion. On the basis of Fick's second law, the experimental glucose concentration profiles in agarose gel are fitted with eq 3. The nonlinear fitting constant, the diffusion coefficient, has been obtained as 5.73×10^{-10} m^2/s, which is close to the result of Andersson et al., who have measured glucose diffusion through 1.2−3.6% (v/v) agarose gel ranging from 4.25×10^{-10} to 6.15×10^{-10} m^2/s at 25 °C using a steady-state diaphram cell.[24] In addition, Li et al.,[25] who have studied the diffusion behavior of glucose in a 0.197% (v/v) agarose gel at a higher temperature 37 °C by measuring the rate of uptake/release from gel cylinders dispersed in a stirred solution of limited volume, obtained diffusion coefficients approximately 50% higher than that determined in this study for 1.5% agarose gel at 25 °C.

The equilibration time of gels in the presence of glucose was also investigated. Figure 4a shows the diffusion kinetic curve of 100 g/L glucose in 0.5% agarose gel at the diffusion distance 0.1 cm. The experimental results are very well described by a time square root transformation, where the fitting diffusion coefficient is 6.26×10^{-10} m^2/s, slightly greater than that in 1.5% agarose gel. This result can be attributed to the less mobility of glucose in a more concentrated hydrogel. Complete equilibration at this diffusion distance is achieved within 200 min. When the polymer volume fraction in the gel increases from 0.5% to 1.5%, as shown in Figure 4b, the equilibration time is prolonged to be within 250 min, resulting from the increased obstruction effect exerted by the increase in the polymer content in the agarose gel.

Diffusion of PEGs in Agarose Gel. To further investigate the effect of the kind of solutes on the diffusion coefficients, a flexible polymer, PEG, was chosen as the solute for diffusion. Figure 5 presents the refractive index change profiles for the diffusion of 50 g/L PEG600 in 1.0% agarose gel at two discrete times: 160 and 310 min. The penetration depth of PEG600 into the agarose gel increases from 0.79 to 0.97 cm, and the refractive index change at diffusion distance of 0.1 cm increases from 1.20×10^{-3} to 1.34×10^{-3} when the diffusion time is extended from 160 to 310 min. Compared with the results of the diffusion of glucose in a more denser network such 1.5% agarose gel mentioned above, it reveals that the diffusion of PEG600 is slower than that of the glucose in the gel. Meanwhile, the experimental concentration profiles of PEG600 obtained according to eq 2 in the agarose gel during the diffusion process are shown in Figure 6. Obviously, the concentration of PEG600 in agarose gel for 310 min is higher than for 160 min for a certain diffusion distance. Figure 6 also compares experimental and predicted concentra-

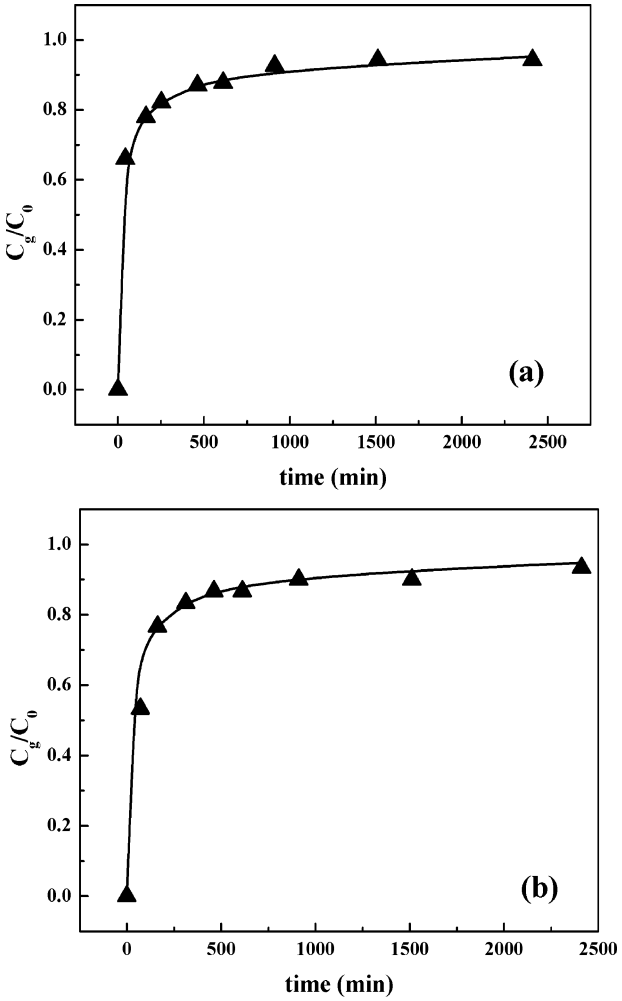

Figure 4. Diffusion kinetics of 100 g/L glucose in (a) 0.5% and (b) 1.5% agarose gel at 25 °C. The lines are calculated from Fick's second law assuming a glucose diffusion coefficient of (a) 6.26×10^{-10} m²/s and (b) 5.73×10^{-10} m²/s.

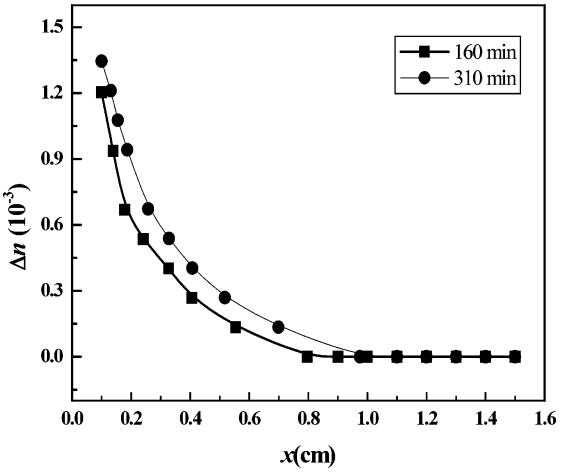

Figure 5. Dependence of the refractive index change on the diffusion distance for the diffusion of 50 g/L PEG600 in 1.0% agarose gel at 25 °C after 160 and 310 min.

tions profiles of PEG600 in the agarose gel. The predicted profiles are based on eq 3 with a fitting parameter $D = 3.35 \times 10^{-10}$ m²/s. The theoretical curve fits the experimental results on the whole.

The interactions between a solute and its surrounding, a polymer network, can generally be described in two different terms, chemical and frictional.[26] The

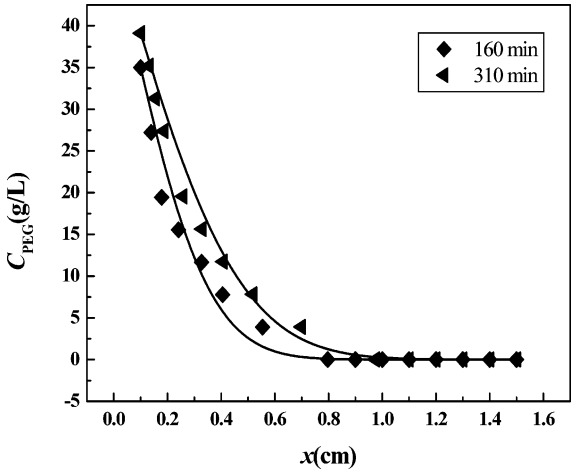

Figure 6. Distribution of the solute concentration as a function of the diffusion distance at three diffusion times for 50 g/L PEG600 in 1.0% agarose gel at 25 °C after 160 and 310 min. The lines are calculated from Fick's second law, assuming a PEG600 diffusion coefficient of 3.35×10^{-10} m²/s.

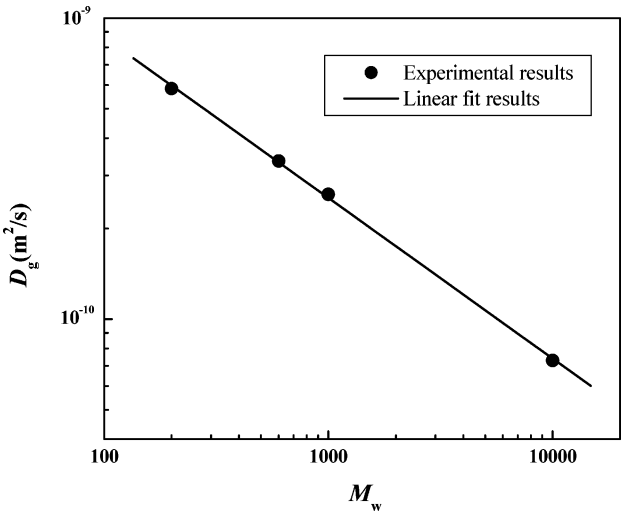

Figure 7. Dependence of the diffusion coefficients (D_g) in 1.0% agarose gel on the molecular weights of PEG samples.

chemical interaction includes attractive forces, which sometimes dominate the diffusion process. The frictional effects, including solvent effects, steric hindrance, and hydrodynamics, influence the diffusion of the solutes in different ways. PEG is a neutral solute, which has no electrostatic interactions with agarose gel networks, and previous research results of detailed structure analysis have revealed that the PEG exists as a helical conformation in aqueous medium while as a random coil chain in benzene.[27,28] However, the PEG molecules penetrate gel networks always through stretching their body, implying that the gel networks have more influence on the transport of PEGs than common small molecules.[8] Moreover, Zhu et al. once have found that there are strong interactions between the PEGs and polymer network by formation of hydrogen bonds in the PVA gels.[29] Therefore, the hydrogen-bonding interactions maybe also exist in our system because there are many hydroxyl groups on the agarose gel network, which might retard the diffusion of PEGs.

Figure 7 shows the different PEG diffusion coefficients in 1.0% agarose gel. The diffusion coefficients of PEGs in the gel are generally in the range of $(0.7-5.9) \times 10^{-10}$ m²/s and decrease with an increase in the

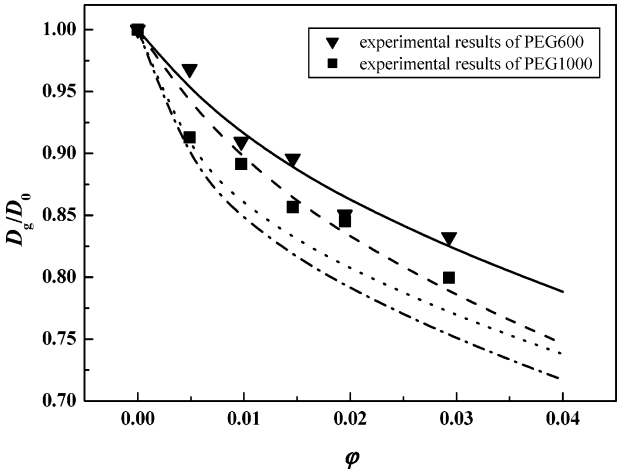

Figure 8. Dependence of the effect of PEG600 and PEG1000 diffusivity on the agarose polymer volume fraction in the agarose gel. The solid line (—) and dashed line (- - -) are obtained from Amsden's model for PEG600 and PEG1000, respectively. The dotted line (· · ·) and dot−dashed line (— · —) are obtained from Ogston's model for PEG600 and PEG1000, respectively.

molecular weight of PEG, indicating a decreased mobility resulted from the increased size of the PEGs. The relationship suggests a simple power law that presents a reasonable description of the solute diffusion coefficient D_g vs molecular weight (M_w) as follows:[8]

$$D_g = kM_w^n \tag{4}$$

where k is a preexponential factor and n is a characteristic exponent. From a linear fitting, k and n are calculated to be 1.01×10^{-8} and -0.533, respectively. The exponent n is close to the value of -0.5, which is characteristic for the negligible solvent drainage coil exhibited in dilute solution, indicating that the conformation of PEGs in agarose gel is in a situation close to the negligible solvent drainage coil.

Role of the Agarose Gel Concentration. The first important factor affecting the diffusion process is the available volume between fibers, namely the diffusion media. As the diffusion of solutes occurs in the liquid channels formed by the polymer phase,[12] an increase in the gel concentration will cause a decrease in the mesh size of the gel network, leading to a shrinkage of the space of these channels available for the diffusing solute and an increase in the path length for diffusive transport and thus an increase of the obstruction effect. Figure 8 presents the dependence of the diffusion coefficients of PEG600 and PEG1000 on the concentration of agarose gel. The ratio D_g/D_0 ranges from 0.79 to 0.96, showing high diffusion coefficients of PEGs in the agarose gels compared with those in pure water. Over the entire range of polymer concentrations, PEG1000 diffuses less rapidly than PEG600 in the hydrogel. At a given agarose concentration, the diffusion coefficients decrease with increasing size of the PEG, indicating an increased retarding effect when the solute size increases. Furthermore, a slightly systematic decrease in diffusion coefficients as a function of increasing agarose concentration in the gels is observed, which is similar to the relationship between PEG600 coefficients and the gel concentration for Curdlan gels.[30] Decreased diffusion coefficients suggested a relatively low mobility. This can be attributed to the fact that the increase in the volume fraction of agarose in the gels reduces the space for the diffusion of PEGs, resulting in the increase of obstruction effects. PEG1000 with a larger M_w encounters a lager obstruction effect than the PEG600 during the diffusion process. It has been reported that the diffusion of nisin decreases in agarose gel when the agarose concentration in gel increases.[31] Bica et al.[5] have also reported that the ratio of diffusion coefficient of the cellulose whiskers in agarose gel to that in the free suspension decreases linearly with the gel concentration, and the slow mode decreases more rapidly than the fast mode.

Analysis of the Diffusion Data with Theoretical Models. During the past several years, many models have been used to explain the diffusion or transport behavior of small molecules, ions, macromolecules, and particles in hydrogels.[32,33] The results have proved that the diffusion process of solutes has very close relationship with the molecular size of the diffusing solutes, mesh size of the gel network, temperature, viscosity, and so on. These theoretical models mainly include the free volume model,[34] hydrodynamic model,[35] and obstruction effect model[36] as well as the model of combination of hydrodynamic drag and obstruction effect.[37] The hydrodynamic models can provide a reasonable explanation for the diffusion behavior in homogeneous hydrogel, whereas the models of obstruction effect are more consistent with the diffusion results in heterogeneous hydrogel.[38] It is well-known that the agarose gel is a kind of typical heterogeneous hydrogel. Therefore, in this work, two models based on obstruction effect, namely, Ogston's model and Amsden's model, were chosen to simulate the diffusion behavior of PEG600 and PEG1000 in agarose gels.

Ogston's model assumes that solute diffusion in hydrogel consists of a series of random unit steps, and the unit step will stop when the solute molecules encounter the hydrogel fiber. Polymer gel is considered to be random networks composed of long and straight fibers, while the diffusing solute is considered to be a hard sphere.[39] This diffusion model takes into account the hydrodynamic radius of the diffusing solute, the hydrodynamic radius of the polymer fiber, and the volume fraction of the polymer matrix. The expression is[39]

$$\frac{D_g}{D} = \exp\left[-\varphi^{0.5}\left(\frac{r_s + r_f}{r_f}\right)\right] \tag{5}$$

where φ is the volume fraction of polymer fibers in the hydrogels and r_f the radius of the polymer fibers.

Amsden's model takes the stiffness of the polymer fibers in the polymer gel into account and assumes that the diffusion of diffusing solutes is realized through finding enough space between polymer fibers. This diffusion model combines the free volume theory with the obstruction and scaling concepts. In this model, the reduction in solute diffusivity is given by[40]

$$\frac{D_g}{D_0} = \exp\left[-\pi\left(\frac{r_s + r_f}{k_s\varphi^{-1/2} + 2r_f}\right)^2\right] \tag{6}$$

where D_g is the diffusion coefficient of diffusing solute in hydrogel and k_s the scaling parameter. As agarose gel fibers contain bimodal bundles of α-helix chains with 87% having a radius of 15 Å and 13% having a radius

of 45 Å,[37] r_f is thus taken to be 19 Å during the application.[38]

According to Johansson's report, M_w of PEG is related to the diffusion coefficient in infinite dilution as follows:[26]

$$D_0 = 7.0 \times 10^{-9} M_w^{-0.46} \quad (7)$$

where D_0 is the diffusion coefficient of PEG in infinite dilution (m^2/s). Therefore, D_0 of PEG600 and PEG1000 can be calculated as 3.69×10^{-10} and 2.92×10^{-10} m^2/s, respectively. Further, the hydrodynamic radii of PEG600 and PEG1000 are obtained respectively to be 6.6 and 8.3 Å by using the following Stokes−Einstein equation:

$$D_0 = k_B T/(6\pi\eta r_s) \quad (8)$$

where k_B is Boltzmann's constant, T the temperature in kelvin, η the solvent viscosity, and r_s the hydrodynamic radius of the diffusing solute.

Meanwhile, it is reported that the gyration radius for PEG can express the effective solute radius in solution better than the hydrodynamic radius.[36] As a highly flexible polymer, the relationship between the gyration radius, r_g, and the hydrodynamic radius of PEG can be expressed as

$$r_g = \frac{3}{2} r_s \quad (9)$$

As a result, the gyration radius of PEG600 and PEG1000 is calculated to be 9.9 and 12.6 Å, respectively. The gyration radius of the PEGs is therefore used in the simulation.

By using both Ogston's and Amsden's model, the experimental diffusion coefficients of PEG600 and PEG1000 obtained for different agarose concentrations at a given temperature are fitted with eq 5 and eq 6, and the results are plotted in Figure 8. It is clear that the results from Ogston's model deviate from the experimental results, which coincides with the report in the literature indicating that Ogston's model is often unsatisfactory for agarose gels.[41] This diffusion model overestimated the influence of polymer concentration on the diffusion coefficients, which might be attributed to the fact that the PEG is a flexible polymer. However, the results predicted by Amsden's model fit the experimental results well when adopting the scaling parameter k_s = 13.4 and 13.1 Å for PEG600 and PEG1000, respectively. The two scaling parameters are close to each other, indicating that it might be characteristic of the agarose gel system. It is reported that the application of Amsden's model to the diffusion of myoglobin, bovine serum albumin, $C_{12}E_8$ micelle, and $C_{12}E_{10}$ micelle in agarose gel produced consistent values of the regression k_s ranging from 10.7 to13.8 Å using 19 Å as the radius of agarose gel fiber.[38] Therefore, the scaling parameters obtained in this work are in good agreement with the reported data, suggesting that the obstruction effect plays a key role in the diffusion of PEGs in agarose gels.

Conclusions

The diffusion coefficients and concentration profiles of glucose and PEGs in agarose gel were successfully in situ determined by the newly established refractive index method. It is shown that glucose can penetrate the agarose gel matrix freely. Further, the results confirm that the diffusion coefficients depend on not only the volume fraction of polymer in the gel matrix but also the size of the diffusing solutes (or the molecular weight of the solutes). Increasing either the concentration of the agarose gel or the size of the solutes results in the decrease of the diffusion coefficient. The relationship between the diffusion coefficients and the molecular weight of PEGs obeys a simple power law with an exponent suggesting that PEGs in agarose gel is in a situation close to the negligible solvent drainage coil. By applying the two typical obstruction models of both Ogston's model and Amsden's model to simulating the diffusion behavior of PEGs, Amsden's model fits well with the experimental results, suggesting that the obstruction effect dominates the diffusion process.

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