Pharmaceutical Research, Vol. 14, No. 10, 1997

Molecular Modeling of Polymers 16. Gaseous Diffusion in Polymers: A Quantitative Structure–Property Relationship (QSPR) Analysis

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Received May 6, 1997; accepted June 20, 1997

Purpose. The purpose of this study was to identify the key physicochemical molecular properties of polymeric materials responsible for gaseous diffusion in the polymers.
Methods. Quantitative structure-property relationships, QSPRs were constructed using a genetic algorithm on a training set of 16 polymers for which CO_2, N_2, O_2 diffusion constants were measured. Nine physicochemical properties of each of the polymers were used in the trial basis set for QSPR model construction. The linear cross-correlation matrices were constructed and investigated for colinearity among the members of the training sets. Common water diffusion measures for a limited training set of six polymers was used to construct a "semi-QSPR" model.
Results. The bulk modulus of the polymer was overwhelmingly found to be the dominant physicochemical polymer property that governs CO_2, N_2 and O_2 diffusion. Some secondary physicochemical properties controlling diffusion,including conformational entropy, were also identified as correlation descriptors. Very significant QSPR diffusion models were constructed for all three gases. Cohesive energy was identified as the main correlation physicochemical property with aqueous diffusion measures.
Conclusions. The dominant role of polymer bulk modulus on gaseous diffusion makes it difficult to develop criteria for selective transport of gases through polymers. Moreover,high bulk moduli are predicted to be necessary for effective gas barrier materials. This property requirement may limit the processing and packaging features of the material. Aqueous diffusion in polymers may occur by a different mechanism than gaseous diffusion since bulk modulus does not correlate with aqueous diffusion, but rather cohesive energy of the polymer.

KEY WORDS: diffusion; polymers; gases; bulk modulus; QSPR.

INTRODUCTION

The permeability of polymeric materials is an important consideration in the pharmaceutical industry. Many pharmaceutical preparations need to be protected from oxygen, water vapor, carbon dioxide and other gaseous penetrants. The polymeric packaging material for the preparation must serve as an effective barrier to gaseous diffusion. In other applications, the polymeric material serves as a core to the controlled release of an active biological agent. Solubility and diffusion of the (usually) small organic biological agent in the polymer matrix is central to the controlled release behavior.

Permeability, P, solubility, s, and diffusivity, d, are related by the relationship

$$P = s * d \tag{1}$$

In this study, we have focused upon diffusivity and in particular, the diffusion coefficient, D, of a particular gas in a particular polymer matrix at a fixed temperature, T. In these systems, gas diffusion is a random kinetic process and the Van't Hoff-Arrhenius relationship holds,

$$D(T) = D_0 \exp(-E_D/RT) \tag{2}$$

where, D_0 is the pre-exponential factor, E_D is the activation energy for diffusion, and R is the gas constant.

The composite characterization of diffusion of gases and small organics in polymers consists of a collection of independent experimental studies on a small number of polymers and diffusing agents for particular applications. There has been little effort in establishing a unified theory/model across a range of polymers of diverse structure and/or a range of penetrant agents. Moreover, molecular mechanisms of diffusion remain largely qualitative descriptions consistent with experimental observations. However, computer-assisted molecular design, CAMD, is a tool which may facilitate the realization of a unified molecular understanding of diffusion. In this paper we report the findings of a CAMD analysis of the diffusion of CO_2, N_2 and O_2 through a set of polymeric materials. The specific CAMD technique used in this study is quantitative structure property relationship, QSPR, analysis (1).

The CAMD approaches that can be used to estimate the diffusion of small penetrant molecules through polymeric materials are theoretical models (2–4), molecular simulations (5–7), QSPR analysis (1,8) and combinations from these three general approaches.

QSPR analysis is the method used in the study reported here. The first step is to assemble the modeling data in the form of a training set. Three types of QSPR training sets can be considered modeling small molecule diffusion in polymers,

i. A training set with one common polymer, a series of diffusing chemical entities, and the corresponding observed diffusion measures.
ii. A training set with a series of different polymers, a single,common diffusing chemical entity, and the corresponding observed diffusion measures.
iii. A training set with different polymers, different types of diffusing chemical entities, and the corresponding observed diffusion measures.

The next step in the QSPR analysis consists of the computation of a trial basis set of physicochemical molecular properties of the polymers and/or diffusing chemical entities. The final step is to establish a statistical relationship between the observed diffusion measures (dependent variable) and members of trial basis set. The most robust and significant statistical relationships,or QSPR models, then serve as guidelines to both understand diffusion processes and to forecast diffusion behavior in new systems.

QSPR models have the capacity to be predictive at the molecular level, are relatively easy to construct, use, and interpret since one can directly evaluate the relative importance of

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Table I. The Training Set of Polymers and Calculated Measures of the QSPR Descriptors for Construction of Diffusion QSPRS for CO_2, O_2 and N_2

Polymer	$-\log D^a$ CO_2	$-\log D$ O_2	$-\log D$ N_2	S cal/mole/°	M AMU	E_d Kcal/mole	E_+ Kcal/mole	E_- Kcal/mole	E_{co} J/cm^3	B 10^9N/m^2	ρ g/cm^3	V_r cm^3/mole
Poly(ethylene terephthalate)	8.83	8.44	8.70	1.96	38.4	−2.59	−2.10	−0.22	540.4	7.4	1.33	144.2
Poly(bispenol-A-carbonate)	8.32	7.68	7.82	0.53	63.5	−4.13	−1.26	−0.53	435.8	5.3	1.20	211.0
Polyoxymethylene	7.62	7.43	7.68	3.30	15.0	−0.86	−1.53	0.69	345.4	7.4	1.25	24.0
cis-1,4-polyisoprene	5.96	5.80	5.96	1.51	26.5	−1.57	0.55	−0.63	308.6	1.8	0.90	75.7
Polystyrene	7.22	6.96	7.22	1.00	34.3	−3.26	−1.09	−0.59	406.8	5.2	1.05	100.6
Poly(ethyl methacrylate)	7.52	6.96	7.60	1.53	26.0	−2.15	−1.79	−0.56	380.1	4.3	1.12	102.4
Polyethylene	6.43	6.34	6.49	4.30	14.0	−1.39	0.45	−0.26	298.5	3.6	0.86	32.9
Polytetrafluoroethylene	7.[illegible]	6.83	7.00	1.48	32.5	−1.69	−1.27	−0.16	343.6	3.6	2.00	49.5
Polybutadiene	5.98	5.82	5.96	2.19	19.5	−1.30	0.93	−0.89	304.8	2.5	0.89	60.7
Polyisobutylene	7.22	7.10	7.30	1.22	28.0	−2.50	0.77	−0.66	237.0	2.6	0.84	66.8
Poly(vinyl chloride)	8.60	7.91	8.40	0.80	31.0	−1.93	−0.90	−0.46	441.7	5.3	1.39	45.2
Poly(vinyl acetate)	7.52	7.30	7.52	2.15	26.3	−1.91	−2.49	0.35	429.3	5.9	1.19	72.2
Poly(dimethyl butadiene)	7.20	6.85	7.07	1.48	33.5	−1.83	0.16	−0.37	316.6	3.2	0.88	89.7
Polychloroprene	6.57	6.37	6.54	1.51	39.6	−2.09	−2.31	0.85	422.1	2.3	1.21	73.7
Poly(2,6-diphenyl-1,4-phenylene oxide)	6.41	6.14	6.37	0.78	61.5	−3.45	−0.88	−0.75	498.0	4.8	1.14	211.7
Poly(dimethyl siloxane)	4.82	4.60	4.82	1.22	37.0	−1.97	−0.31	0.29	213.8	0.7	0.98	75.6
						Error[b]	±6.1%	±5.8%	±3.8%	±4.6%		

[a] D is in cm2/s at 25°C.

[b] Error refers to the average error of predicting a property using the Van Krevelen GAP method.

the various physicochemical molecular properties in the model. A QSPR model, on the other hand, is only as good as the training set and corresponding computed physicochemical molecular properties from which it is derived. Further, it may not provide mechanistic insight.

QSPR approaches have been used to predict several polymer properties including diffusion and other transport measures. Combinations of the three approaches described above, theoretical, simulation and QSPR analysis can be used. Most likely, simulation generated physicochemical property measures are used as a part of the trial basis set of independent variables to construct a QSPR, as well as to attempt to elucidate the molecular mechanism of diffusion.

METHODS

Dependent Measures

The training set used to construct the diffusion QSPR models consists of sixteen polymers. The dependent variable is log D, where D is the measured diffusion constant for a simple gas diffusing through each of the polymer matrices at 25°C (9). Carbon dioxide (CO_2), oxygen (O_2) and nitrogen (N_2) are the three gases which have been modeled in this study. Table I provides a list of the polymers and the respective log D values for CO_2, O_2, and N_2.

Aqueous diffusion in polymeric materials is important to study and model, but comparable experimental data in the open literature is quite limited. Six polymers for which aqueous diffusion under common conditions has been measured (9) was assembled and used in "semi-QSPR" analysis as part of this investigation.

Clearly, our QSPR modeling would benefit from larger training sets of diffusion measures in polymers. Unfortunately, the training sets reported here are the best sets of comparable data we could assemble.

Independent Measures

Nine physicochemical properties were considered as the trial basis set of independent variables. These properties, their descriptions and symbols are listed as part of Table II. Torsion angle unit, TAU, theory (10) was used to compute S, M, E_d, E_+, E_-. S is the torsion angle conformational entropy of the monomer repeat unit. S reflects the conformational freedom (molecular flexibility) available to the polymer chain. M is the monomeric molecular mass of the polymer, and is used to measure the ease/difficulty of moving/displacing a polymer

Table II. The Parent Set of QSPR Diffusion Descriptors for the Polymer Training Set

Characteristic	Descriptor	Symbol(s)
Intrachain flexibility	Conformational entropy	S
	Monomer molecular weight	M
Interchain flexibility	Bulk modulus	B
	Cohesive energy density	E_{co}
Intrinsic molecular free volume	Amorphous/rubbery density	ρ
	Rubbery molar volume	V_r
Polymer matrix—diffusing agent interaction	Molecular field of the polymer chain	
	• Dispersion field	E_d
	• Positive charge field	E_+
	• Negative charge field	E_-

chain segment. E_d, E_+, and E_- are the monomer molecular field descriptors for the polymer generated using steric, positive charge and negative charge probes, respectively. These descriptors model the potential field of a monomer, and, hence, the local intermolecular interaction profile of the polymer chain.

The Van Krevelen group additive property, GAP, approach was used to calculate E_{co}, B, ρ, and V_r (11). E_{co} is a the cohesive energy density which measures the polymer matrix packing energy per unit volume. The square root of E_{co} is the solubility parameter. B is the bulk modulus of the amorphous form of the polymer, and is a measure of the elasticity of the polymer matrix. ρ and V_r are the density and molar volume of the rubbery state, respectively, of the (amorphous) polymer. These descriptors were selected in order to provide a comprehensive trial basis set of properties which could reasonably be expected to be related to diffusion behavior.

D is an intensive material property while M and V_r are extensive properties. This mixing of property types can be "justified" in the spirit of QSPR analysis where property descriptors in a QSPR model can be "masked variables" reflecting behavior different from their direct interpretation. For example, we view the role of monomer molecular weight, M, as refelcting ease/difficulty of kinetic segmental motion in the polymer matrix.

Statistical Methods

Multivariate linear regression, MLR, analysis and construction of data set cross-correlation matrices were used to evaluate trial QSPR models. The Genetic Function Approximation, GFA, (12) a genetic algorithm, GA, (13), was applied to three training sets containing log D values for CO_2, O_2, and N_2. GFA is a hybrid of the Hollands GA (14) and the Multivariate Adaptive Regression Splines (MARS) (15) algorithms. By combining the MARS and GA approaches, one is able to significantly reduce the large function space that MARS explores, while simultaneously making effective use of the GA to more fully combine trial basis set descriptors. The general procedure used to evolve the QSPR diffusion models is given in reference (16). The GFA experiments for diffusion modeling were carried out using both linear and quadratic descriptor terms in the trial basis sets. The smoothing factor *d* (12) was assigned a value of "1". The GFA experiments were monitored for 10,000 crossovers in order to ascertain convergence of independent variable usage during QSPR model evolution. In each case the cross-correlation descriptor matrix was examined to eliminate trial QSPRs in which pairs of unique descriptors had cross-correlation coefficients greater than 0.50. Analogs were considered outliers when the difference in predicted and observed energies equaled or exceeded 2.0 standard deviations from the mean. Regression analyses were performed minus the outliers and examined to see if significant improvements in the regression equations resulted.

RESULTS

The calculated values for the physicochemical molecular properties, the trial basis set molecular descriptors, for each of the polymers under investigation are listed in Table I. This table also reports average estimation errors using the Van Krevelen GAP method (11) by comparing calculated to observed values for some of the polymers in the training set. The absolute average errors of estimation are approximately 6.1%, 5.8%, 3.8% and 4.6% for E_{co}, B, ρ, and V_r, respectively.

The composite training dataset containing the trial basis set of QSPR molecular descriptors and the observed −log D values for the three diffusing gases was first investigated for linear pairwise variable cross-correlation. Table III contains the cross-correlation coefficients (R) for individual pairs of variables. This analysis indicates significant correlations, that is high correlation coefficient values of 0.81, 0.82, and 0.83 between bulk modulus, B, and the −log D values of all three penetrants, viz., CO_2, N_2 and O_2, respectively. E_{co} is the next most significant linear correlation descriptor with −log D having moderate correlation coefficients of 0.65 for CO_2, 0.63 for N_2 and 0.62 for O_2. E_+ has the third most significant linear correlations with the −log D with negative correlation coefficients of −0.50, −0.51, and −0.49 for the −log D, of CO_2, N_2 and O_2, respectively. The −log D values of CO_2, N_2 and O_2 have high cross-correlations to one another. For example, the cross-correlation coefficient for the −log D values of N_2 and O_2 is 0.99. There are also significant cross-correlations among some of the descriptors including E_d and S (0.67), E_d and M (−0.87) and E_{co} and E_+ (−0.71).

GFA analysis of CO_2 as a gas penetrant leads to QSPR diffusion models with both linear and quadratic terms. The top two- and three-descriptor QSPR diffusion models are reported in Part A of Table IV. These models were selected on the combined basis of their R^2 values and least squares error terms (LSE). The top three-descriptor model has an R^2 value of 0.74 and a LSE of 0.27. This diffusion model shows B as the dominant descriptor, consistent with the cross-correlation analysis, and S also making a meaningful contribution. Those descriptors appearing in quadratic form in the QSPR equations are characterized by specifying their extrema values at the bottom of each model summary. The "(max)" or "(min)" indicates if the extremum value maximizes or minimizes the descriptor's impact on −log D. The polymer, poly(2,6-diphenyl-1,4-phenylene oxide) is an outlier of eq. 2 in Part A of Table IV. If this polymer is eliminated from eq. 2, the new model, represented by eq. 3, with an R^2 value of 0.87 and a LSE of 0.14 results.

The top two- and three-descriptor QSPR diffusion models generated for N_2 diffusion by GFA analysis are reported in Part B of Table IV. These models have R^2 values of 0.71 and 0.74 and LSE values of 0.26 and 0.24, respectively. Once again B is the dominant descriptor. S is the other significant descriptor. The polymer, poly(2,6-diphenyl-1,4-phenylene oxide) is a marginal outlier of eq. 2 in Part B of Table IV. If this polymer is eliminated from eq. 2, the new model, represented by eq. 3, with an R^2 value of 0.86 and a LSE of 0.13 results. Extremum values of B were calculated and are reported for each of the three QSPR models in Part B of Table IV.

QSPR diffusion models were also evolved for O_2 using GFA. The top two- and three-descriptor QSPR diffusion models generated for O_2 diffusion by GFA analysis are reported in Part C of Table IV. In these equations, B is once again the most significant independent variable while S is the second most significant descriptor. The polymer, poly(2,6-diphenyl-1,4-phenylene oxide) is an outlier of eq. 2 in Part C of Table IV. If this polymer is eliminated from eq. 2, the new model, represented by eq. 3, with an R^2 value of 0.85 and a LSE of 0.13 results.

Table III. Cross-Correlation Matrix for the QSPR Descriptors and Log D Values

	S	M	E_d	E_+	E_-	E_{co}	B	ρ	V_r	−log D (CO_2)	−log D (N_2)	−log D (O_2)
S	1											
M	−0.73	1										
E_d	0.67	−0.87	1									
E_+	0.11	−0.27	0.23	1								
E_-	0.33	−0.17	0.36	−0.57	1							
E_{co}	−0.24	0.51	−0.49	−0.70	0.00	1						
B	0.16	0.07	−0.19	−0.60	0.11	0.71	1					
ρ	−0.17	0.19	−0.02	−0.58	0.26	0.41	0.37	1				
V_r	−0.56	0.90	−0.88	−0.22	−0.37	0.57	0.22	−0.01	1			
−log D (CO_2)	−0.12	0.14	−0.29	−0.50	−0.05	0.65	0.81	0.39	0.21	1		
−log D (N_2)	−0.03	0.07	−0.24	−0.49	−0.01	0.62	0.83	0.39	0.15	0.99	1	
−log D (O_2)	−0.06	0.05	−0.23	−0.51	−0.02	0.63	0.82	0.39	0.14	0.99	0.99	1

GFA crossover plots associated with the evolution of optimizing the QSPR diffusion models of CO_2, N_2 and O_2 are given in Figure 1. Each curve of descriptor usage versus crossover operation number reaches a plateau after about 4000 crossovers in the GFA experiments which indicates a convergent optimization of each of the QSPR models. Thus, the models reported in Table IV are the respective "best" models that can be realized for the trial basis sets (descriptors) used in the experiments.

The bulk modulus, B, is the only independent variable used in more than 80% of the QSPR models during optimization by the evolution process of GFA for all three gases. B is also the most significant QSPR descriptor for all three gases and appears as a linear term and in most cases as a quadratic term in the optimized (best) QSPR models for each gas. Consequently, the values of B(max) in the three optimized gas diffusion QSPR models reflect the comparative impact of B on −log D. That is, the values of B(max) in eqs. 2 and 3 in Table IV, Parts A–C permit a comparison of the differences among the three gases due to the bulk modulus of the polymer matrix. Oxygen is predicted to be least retarded (greatest value of B(max) predicted) in diffusion, while CO_2 and N_2 are predicted to be very similar in diffusion behavior, as governed by B, since their B(max) values are nearly the same.

Table IV. The Top Two- and Three-Descriptor QSPR Diffusion Models For A) CO_2, B) N_2 and C) O_2 Derived from the GFA Analysis

Part A: **For CO_2 gas as a penetrant**

1. $-\log D = 5.64 + 0.46\,B - 0.27\,S$
   $N = 16$ $R^2 = 0.71$ $LSE = 0.29$
2. $-\log D = 4.97 + 0.82\,B - 0.04\,B^2 - 0.24\,S$
   $N = 16$ $R^2 = 0.74$ $LSE = 0.27$
   $B(max) = 9.53$
3. $-\log D = 4.97 + 0.82\,B - 0.04\,B^2 - 0.24\,S$
   $N = 15$ $R^2 = 0.87$ $LSE = 0.14$
   $B(max) = 8.25$

Part B: **For N_2 gas as a penetrant**

1. $-\log D = 4.59 + 0.83\,B - 0.05\,B^2$
   $N = 16$ $R^2 = 0.71$ $LSE = 0.26$
   $B(max) = 8.54$
2. $-\log D = 4.91 + 0.79\,B - 0.04\,B^2 - 0.16\,S$
   $N = 16$ $R^2 = 0.74$ $LSE = 0.24$
   $B(max) = 9.42$
3. $-\log D = 4.82 + 0.95\,B - 0.06\,B^2 - 0.25\,S$
   $N = 15$ $R^2 = 0.86$ $LSE = 0.13$
   $B(max) = 8.21$

Part C: **For O_2 gas as a penetrant**

1. $-\log D = 4.51 + 0.77\,B - 0.04\,B^2$
   $N = 16$ $R^2 = 0.72$ $LSE = 0.23$
   $B(max) = 8.89$
2. $-\log D = 4.77 + 0.73\,B - 0.04\,B^2 - 0.13\,S$
   $N = 16$ $R^2 = 0.73$ $LSE = 0.22$
   $B(max) = 9.73$
3. $-\log D = 4.97 + 0.88\,B - 0.05\,B^2 - 0.22\,S$
   $N = 15$ $R^2 = 0.85$ $LSE = 0.13$
   $B(max) = 8.39$

Aqueous diffusion measures at T = 25°C were found in the literature for the six polymers listed in Table V. The nine physicochemical properties given in Table II, and used in the gas diffusion QSPR analyses, were employed to construct a "semi-QSPR" model using step-wise linear regression analysis. Six observations, polymers, is not a large enough training set for the meaningful application of GFA. No significant correlation was found between −log (D) for aqueous diffusion and any one, or combination of two, of the nine physicochemical properties in Table I. Thus, we estimated other physicochemical properties including the cohesive energy, E'co, of the polymer using the Van Krevelen method. −Log D of aqueous diffusion has a strong correlation with E'co, the R^2 value being 0.78 for the six polymers in Table V. There is a moderate correlation between bulk modulus, B, the principal correlation property found for gaseous diffusion, and E'co, with $R^2 = 0.48$. $R^2 = 0.16$ for the correlation between aqueous log D and B for the six polymers of Table V.

DISCUSSION

The most distinct finding from this QSPR analysis is that the bulk modulus, B, of the polymeric material is far and away the dominant polymer property which controls gaseous diffusion in the material. This is not surprising in some ways since intuitively the elasticity of a material would seem related to how it "absorbs" other entities. However, it is surprising that bulk modulus is so very dominant in the diffusion behavior, and that other properties, also intuitively thought to be related to diffusion control and to bulk modulus, such as cohesive energy density, are not often found in the optimized QSPR models.

Little room for selective diffusion design is possible from an analysis of the QSPR models of Table IV. The overwhelming influence of B limits the potential of using other physicochemical properties to fine-tune diffusion behavior. As one would expect, the positive value of the cross-correleation coefficient between B and −log (D) indicates that diffusion decreases as bulk modulus increases. The "problem" with the dominance of B in controlling gaseous diffusion is that diffusion selectivity (the slight difference between values of B(max) for the three gases in corresponding eqs. 2 and 3 in Table IV, indicates selectivity) is enhanced at the expense of a diminished rate of diffusion as represented by −log D. Dispersion field potential, E_d, negative field potential, E_-, and monomer mass, M, each appear in other, slightly less significant, QSPR models than those reported in Table IV for all three gases. M is found to have a positive linear relationship whereas E_d and E_- have a negative linear relationship with −log D for all three gases in these models. The regression coefficients indicate a slightly greater influence of these descriptors on −log D for CO_2 than O_2 or N_2.

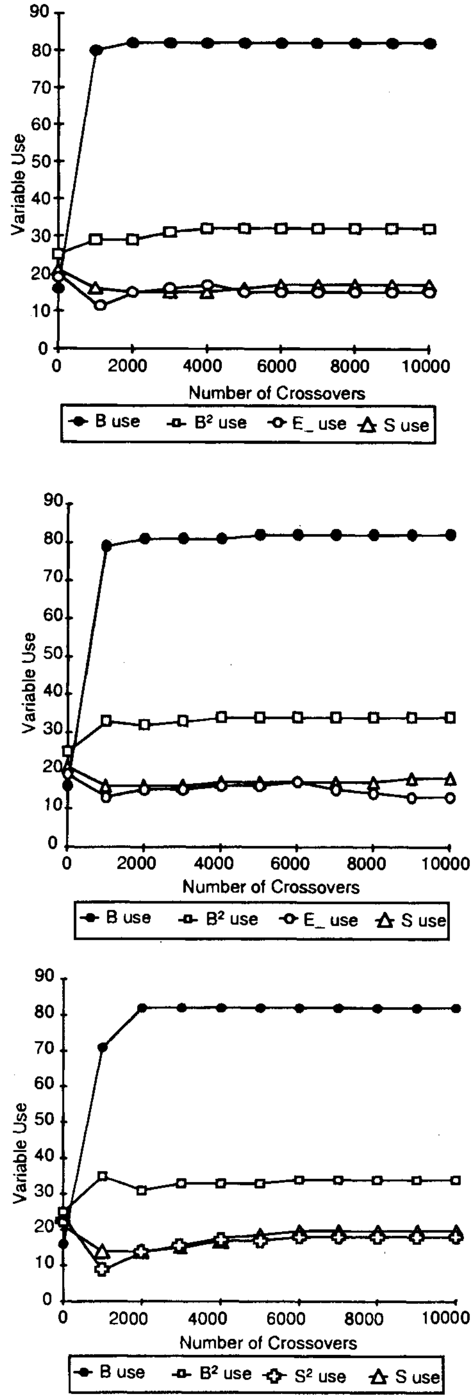

Fig. 1. The GFA optimization plot of crossover operation number versus descriptor usage in the evolving QSPR models for A) CO_2, B) N_2, C) O_2. Variables for which the use is not greater than 15 at any point of the GFA optimization are not included in the figure.

Table V. The Aqueous Diffusion Measures, Log D, for T = 25°C for Six Polymers and the Corresponding Bulk Modulus, B, and Cohesive Energy, E'co, Estimated Values

Polymer	−log D H_2O	B 10^9 N/m^2	E'co J/mol
Poly(ethylene terephthalate)	8.41	7.4	60340
Poly(ethyl methacrylate)	6.98	4.3	31870
Polyethylene	6.64	3.6	9880
Poly(methyl acrylate)	6.92	3.9	24690
Poly(ε-caprolactam)	9.01	5.1	65950
Poly(vinyl alcohol)	8.90	3.5	43190

Perhaps the objective of the analysis should be to identify how to minimize the −log D of O_2. After all, O_2 is considered to be one of the major sources of contamination and deterioration. Unfortunately, the QSPR models constructed in this analysis do not provide a hypothesis for limiting O_2 diffusion in polymeric materials other than to suggest increasing bulk modulus.

The "semi-QSPR" model developed for aqueous diffusion for six polymers may indicate a different diffusion "mechanism" for water as compared to the three gases studied. Aqueous diffusion correlates with cohesive energy of the polymer, but not bulk modulus. Bulk modulus and cohesive energy moderately correlate with one another. Cohesive energy is often associated with the *intrinsic stability* of the polymer matrix, whereas bulk modulus is associated with the capacity to *deform* the polymer matrix. These core property differences may provide "windows" to identifying possible mechanistic differences in diffusion.

Finally, the good news from this analysis is, a) the successful generation of statistically significant diffusion QSPR models, and b) the identification of bulk modulus as the controlling physicochemical property for gaseous diffusion. The bad news is that it does not seem likely to be able to identify a polymeric material with low bulk modulus so as to be useful in packaging and other applications, yet have some other property, like a large cohesive energy density which is highly correlated with the bulk modulus, to limit gaseous diffusion, especially by O_2. The unresolved news is that the limited QSPR modeling of aqueous diffusion in polymers is suggestive of a diffusion mechanism different from that of gaseous diffusion.

ACKNOWLEDGMENTS

Resources of the Laboratory of Molecular Modeling and Design were used to perform this study. The latter part of this study was funded by a contract from Sandia National Laboratories, LD-9687. We appreciate the helpful discussions with Richard Judson formerly of Sandia.

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