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A Revised MM2 Force Field for the Normal Mode Vibrational Analysis of Glucopyranose

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Synopsis. A revised MM2 force field is developed for the study of normal mode dynamics of glucopyranose. The revised potential function is found to reproduce the vibrational spectrum and equilibrium structure of D-glucopyranose better than the original parameter set.

Recent developments in computing power and molecular mechanics force fields have resulted in new interests in the computer modeling of carbohydrates.[1] The potential energy functions used must be an adequate approximation of the actual molecular energy in carbohydrates. It would be desirable to be able to apply molecular mechanics calculation to problems that are related not only to static properties of carbohydrate molecules, but also to their molecular dynamics. Such calculation requires potential functions in which all atoms are explicitly included and whose parameters are optimized not only for the structure of the molecules, but also for their dynamic properties represented by molecular vibration.

We report here an attempt to develop a novel potential energy function to describe the dynamics of glucopyranose in an all atom representation that uses the atomic partial charges determined by ab initio calculations[2] to give reasonable descriptions of hydrogen bonding. Our basic strategy is to reparametrize the MM2 force field[3] with keeping the original functional forms unchanged. The MM2 force field was selected because it has succesfully applied to various structural problems of carbohydrates.[4] It will be shown that both structural and vibrational characteristics of D-glucopyranose are better reproduced by the revised force field than by the original one.

Methods

In developing new potential energy parameters, the procedure used was a systematic optimization of the force constant by fitting the calculated vibrational and structural properties to experimentally determined ones for the prototypical of carbohydrate molecules, D-glucopyranose. For the calculations reported herein, the vibrational spectrum of D-glucopyranose reported by Sookhee et al.[2] and its crystal structure reported by Brawn et al.[6] were referred as experimental data.

The potential energy is a function of bond length b, bond angle θ, torsion angle ϕ, and interatomic nonbonded separation r, [3] as shown in Eq. 1.

$$V(q) = \Sigma K_b(b-b_0)^2 + \Sigma K_\theta(\theta-\theta_0)^2 + \Sigma K_\phi(1+(-1)^{n-1}\cos n\phi) + \Sigma K_{\mathrm{sb}}(\theta-\theta_0)(b-b_0) + \Sigma A_{ij}(K_{\mathrm{a}}\exp(b/r) - K_{\mathrm{b}}/r^6) + \Sigma(q_iq_j/\varepsilon r_{ij}) \qquad (1)$$

where b_0 is the minimum energy bond length, θ_0 is the minimum energy bond angle, n is a periodicity number, r_{ij} is the interatomic separation between atoms i and j, q_i and q_j are atomic partial charges reported by Vasko et al.,[5] and K_b, K_θ, and K_ϕ are the force constants to be determined.

In order to calculate the normal mode frequency, one must solve a complete analytical solution to the equations of motion subject to the assumption that the potential energy of the system can be approximated as a quadratic function.[7]

$$\boldsymbol{HA\Lambda} = \boldsymbol{FA} \qquad (2)$$

where $\boldsymbol{\Lambda}$ is diagonal, i.e. the frequencies of vibration of the system and $\boldsymbol{A}$ is a matrix representation of the eigenvectors to be solved. $\boldsymbol{F}$ and $\boldsymbol{H}$ are the matrices of the second derivatives for the potential energy, represented by Eq. 1, and for the kinetic energy, respectively. In our present study, these second derivatives are calculated with respect to the cartesian coordinates of each atom. Then, the matrix $\boldsymbol{H}$ becomes diagonal with each element being the corresponding atomic mass. Furthermore, the second derivatives for the potential energies are calculated analytically, resulting in rapid and accurate calculation of these quantities. In order to debug our fortran program especially for the second derivative calculation, the present method was first applied to a few simple compounds including diatomic and triatomic molecules, and the resulting data were compared with our pre-calculated values. In order to solve the Eq. 2 for $\boldsymbol{A}$ and $\boldsymbol{\Lambda}$, the subroutine ¥DEF1M in mathematical subprogram library II, released from Hitachi, Ltd. (Japan), was used.

In order to correctly assign the calculated normal mode frequencies to the corresponding experimental ones, the following procedures were carried out:

(1) The structure of D-glucopyranose was optimized.

(2) Minimum energy bond lengths b_0 and angles θ_0 were taken to be the average values observed in the D-glucopyranose crystal, and were not changed during the parameter optimization. These values are listed in Tables 1 and 2.

(3) The force constants K_b, K_θ, and K_ϕ were varied in interval of 0.05, in order for the calculated frequency data to achieve the best fit to the experimental data for D-glucopyranose. Generally, the calculated frequency varies nonlinearly as each force constant was increased (or decreased). Then, the optimum value of each force constant can be regarded as the value minimizing the difference between the experimental and calculated vibrational frequencies for the normal mode of interest.

(4) These parameter values were further refined by varying the three kinds of force constants simultaneously.

(5) The structure of D-glucopyranose was optimized using the parameter set determined above. If the optimized structure was not close to the experimental structure, the steps (3) and (4) were repeated again.

Table 1. Final Potential Energy Parameters, K_b and b_0, for Bond Stretches Energy

Bond type	K_b/md Å^{-1}		b_0/Å	
	Present work[a)]	Original[b)]	Present work[a)]	Original[b)]
O–H	6.60	4.60	0.960	0.942
C–H	4.75	4.60	1.121	1.113
C–C	4.40	4.40	1.528	1.523
C–O	4.40	5.36	1.423	1.407

a) These values were taken from the experimental data of the D-glucopyranose crystal.[5)]
b) Original MM2 parameters cited from Ref. 3.

Table 2. Final Potential Energy Parameters, K_θ and θ_0 for Bending Energy

Angle type	K_θ/mdÅrad^2		θ_0/degree	
	Present work[a)]	Original[b)]	Present work[a)]	Original[b)]
C–C–C	0.430	0.450	110.875	109.470
C–C–H	0.650	0.360	108.782	109.390
C–C–O	0.950	0.700	109.727	107.500
C–O–C	0.950	0.770	113.700	106.800
C–O–H	0.640	0.350	109.220	106.900
H–C–O	0.540	0.540	109.275	106.700
H–C–H	0.350	0.320	107.600	109.400
O–C–O	0.580	0.560	111.500	108.500

a) These values were taken from the experimental data of the D-glucopyranose crystal.[5)]
b) Original MM2 parameters cited from Ref. 3.

Results and Discussion

The set of force constants obtained from the above optimization procedure are listed in Tables 1 and 2, along with the original parameter set.

The stretching constants, K_b, of the O–H and C–H bonds are larger than the corresponding original values. On the contrary, the constant of the C–O bond is fairly smaller than the original, reflecting the structural characteristics of the pyranose ring. The bending constants, K_θ, for C–C–H and C–O–H are fairy larger than the original values. The bending constant for the pyranose ring, C–O–C, is significantly larger than the original value. In our present work, the torsional terms are not changed from the original values, because these terms did not largely influence the calculated data.

The difference in normal-mode frequencies between the experimental and calculated values for D-glucopyranose, obtained by using the parameter set listed in Table 1, are given in Fig. 1, along with those obtained by using the original parameter set. In this figure, mode number was given for each normal mode in order of increasing frequency. As can be seen from Fig. 1, the new potential energy function better reproduces the experimental data than the original parameter set, especially in a high frequency region (from 57 to 66 in the mode number), corresponding to modes primarily involving C–H and O–H stretches. In this region, the rms deviation between the experimental and calculated frequencies is 354.03 cm^{-1} when the frequencies were calculated using the original parameter set, while the corresponding value for the new parameter set is 25.68 cm^{-1}. And in a low frequency region (from 1 to 10 in the mode number), the rms deviation for the original parameter set is 38.28 cm^{-1}, while that for the new parameter set is 26.26 cm^{-1}. Consequently, the new parameter set again exhibits a better reproduction than the original one.

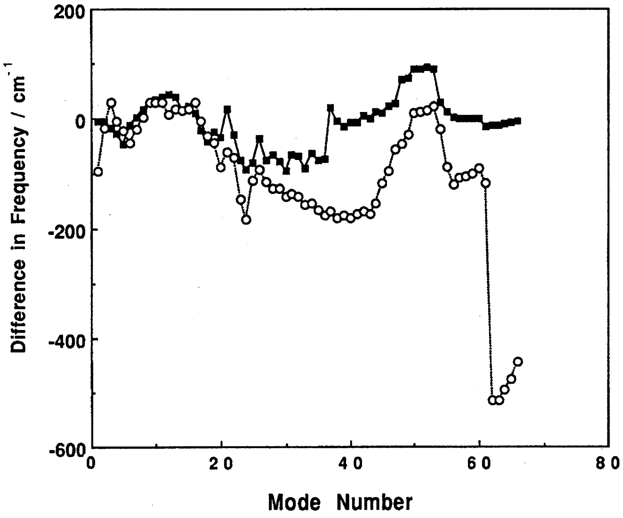

Fig. 1. Comparison of experimental with calculated vibration frequencies. The frequency difference was obtained by subtracting calculated value from experimental one. ○ : Present work. ■ : Obtained by using original parameters of MM2.

The finally-determined structure for D-glucopyranose, is shown for the selected internal coordinates in Table 3, along with the corresponding crystal values. As similar

Table 3. Comparison between the Calculated and Experimental Structure of D-Glucopyranose

Angle	Original[a)] (degree)	Present work[b)] (degree)	Experiment[c)] (degree)
C1–C2–C3–C4	−57.0	−53.9	−51.3
C2–C3–C4–C5	55.5	55.0	55.3
O1–C1–C2–C3	−57.2	−58.1	−68.7
O2–C2–C3–O3	59.4	59.6	63.2
O5–C1–C2–C3	60.5	53.0	54.1
C1–C2–C3	108.2	109.5	111.1
C2–C3–C4	108.1	110.2	109.8
C3–C4–C5	110.6	110.8	111.1
C4–C5–C6	112.1	112.6	111.5
O3–C3–C4	108.2	109.5	110.6
O4–C4–C5	109.4	109.9	110.9
O5–C1–C2	110.6	111.7	110.1

a) These values were calculated by using original MM2 parameters. b) These values were calculated by using final parameters in this work. c) These values were taken from the experimental data of the D-glucopyranose crystal.5)

to the case of vibrational frequency, the new parameter set gives the results closer to the experimental values than those given by the original parameter set. Particularly, the structural parameters characterizing the pyranose ring, namely the C1–C2–C3–C4 and O5–C1–C2–C3 dihedral angles, and the C1–C2–C3 and C2–C3–C4 bond angles, are remarkably improved.

In conclusion, it is expected that the new parameter set better reproduces not only the structural properties of glucopyranose, but also their dynamic properties. As a future development of this study, it is of interest to perform molecular dynamics calculation of carbohydrates, composed of glucopyranose, with the present parameter set.

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References

1) A. D. French and J. W. Brady, "Computer Modeling of Carbohydrate Molecules," American Chemical Society, Washington, DC(1990), Chap. 1.

2) N. H. Sookhee, A. Giammona, M. Field, and J. W. Brady, *Carbhydr. Res.*, **180**, 207(1988).

3) N. L. Allinger, *J. Am. Chem. Soc.*, **99**, 8127(1977). Recently, the MM2 force field has been updated by Allinger et al. (*J. Am. Chem. Soc.*, **111**, 8551(1989)). Using the new force field (MM3), one can perform vibrational analysis for organic molecules including carbohydrates (*J. Am. Chem. Soc.*, **111**, 8566(1989)). In a future study, it is of great interest to compare the present results with those from the MM3 calculation.

4) For example: a) M. J. Sherrod, *Carbohydr. Res.*, **192**, 17(1989); b) A. F. D. deNamor, R. Traboulssi, and D. F. V. Lewis, *J. Chem. Soc., Chem. Commun.*, **1990**, 751; c) M. Ohashi, K. Kasatani, H, Shinohara, and H. Sato, *J. Am. Chem. Soc.*, **112**, 5824(1990).

5) P. D. Vasko, J. Blackwell, and J. L. Koeng, *Carbhydr. Res.*, **19**, 297(1971); **23**, 407(1972).

6) G. M. Brown and H. A. Levy, *Acta Crystallogr. Sect. B*, **35**, 656(1979).

7) M. Levitt, C. Sander, and P. S. Stern, *J. Mol. Biol.*, **181**, 423(1985).