HYDROGEN BONDING IN DNA BASE COMPLEXES

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ABSTRACT Experimental intermolecular frequencies in the DNA base complexes 1-methylthymine (1-MT) and cytosine monohydrate (CMH) are analyzed in terms of simple analytic interatomic potentials. Calculations with two different values for the constants of the nonbonded interactions are considered, and the hydrogen bond potentials are determined for each of these models. The observed frequencies in 1-MT are reasonably well described, although corresponding potentials are very different in the two models. The observed frequencies in CMH are less well described, although corresponding hydrogen bond potentials are similar in the two models. Hydration interactions are found to be important in CMH and the role of the water molecule is discussed. Possible reasons for the shortcomings of this simple analysis are considered.

INTRODUCTION

The conformations and functions of large biological macromolecules are determined by their interatomic potentials. The same potentials determine the frequencies of the normal modes of vibration of such molecules so that if the interatomic potentials are known, the vibration frequencies may be calculated by standard procedures. Calculations have recently been made for several macromolecules (Eyster and Prohofsky, 1974*a,b;* Eyster and Prohofsky, 1977; Lu et al., 1977; Lu et al., 1979). Conversely, if the normal-mode frequencies can be measured experimentally, then information about the interatomic potentials may be derived by analysis of these data. Unfortunately, biological macromolecules are so complex that it is usually difficult to measure the complete spectrum of normal modes and, if the spectrum could be measured, it would be so complex that an interpretation and direct analysis of such data would be impractical at present. An alternative approach is then to consider the smaller functional groups that compose the macromolecules. These groups are themselves molecular units and their modes of vibration can be measured in complexes other than the macromolecules. The normal-mode spectra of these functional groups are much simpler than those of the macromolecules and analysis of the spectra to determine the inter- and intramolecular potentials is more tractable. The potentials derived for the constituent groups are then assumed to be transferable, with the group, to the environment in the macromolecule. Experimental evidence for this assumption of transferability is provided by the similarity in the longitudinal velocity of sound propagating normal to the layers in 1-methylthymine (Martel and Powell, 1976) in cytosine monohydrate (Martel et al., 1977) and in oriented DNA (Maret et al., 1979). The assumption has also been extensively used in discussions of the structure and packing of macromolecules (Momany et al., 1974).

The four bases of DNA crystallize into various complexes that show structural features and, by implication, normal modes of vibration similar to those of the bases in DNA itself.

Many of these complexes have layer-type structures in which the purine or pyrimidine rings lie in planes separated by ~3.4 Å, as in DNA itself. Consequently, analysis of the normal modes of relatively simple complexes may provide information about intermolecular potentials that can be transferred with the corresponding base into similar molecular environments, e.g., those in which the base is attached to the DNA backbone.

In this paper we analyze some experimental intermolecular mode frequencies at the Γ point (i.e., the point at zero wave vector) for two DNA base complexes, 1-methylthymine (1-MT) and cytosine monohydrate (CMH). The analysis is used to determine the parameters of simple hydrogen bond potentials in the two complexes, and to examine the possible role of the water molecule in CMH.

The crystal structures of both 1-MT (Hoogsteen, 1963; Kvick et al., 1974) and CMH (Jeffrey and Kinoshita, 1963; McClure and Craven, 1973) have been determined by diffraction methods. Both solids crystallize in a monoclinic lattice (space group $P2_1/c$) with four molecules, of 1-MT or CMH arranged in layerlike structures, in the respective unit cells. In 1-MT the molecular layers are almost parallel to the (102) lattice planes while in CMH the layers containing the cytosine molecules are parallel to the (308) planes. In both cases the layer separation is ~3.4 Å. To discuss the hydrogen bond systems in the two crystals, we use the notation of Kvick et al. (1974) for 1-MT and of Jeffrey and Kinoshita (1963) for CMH. In 1-MT the molecules are linked in pairs within a layer by two $N_3—H_1\cdots O_9$ bonds to form hydrogen-bonded dimers. Dimers within the same layer are linked by a $C_6—H_2\cdots O_8$ hydrogen bond (Kvick et al., 1974), but there is no hydrogen bonding between the molecular layers. In CMH the hydrogen bonds $N_3—H_3\cdots N_1$ and $N_6—H_6\cdots O_2$ link the cytosine molecules within a layer into parallel ribbons along the b axis. The water molecules lie between the layers and three hydrogen bonds to the water molecule from different cytosine molecules link the ribbons of cytosine molecules into a three-dimensional hydrogen-bonded network. The crystal structures of CMH and 1-MT are shown in Fig. 1.

Optical measurements of the intermolecular mode frequencies at Γ have been made for 1-MT by Harada and Lord (1970) and more completely by Kirin et al. (1975). Harada and Lord interpreted their results in terms of two simplified force models, while Kirin et al. used 11 Buckingham potentials for the nonbonded interactions and a three-parameter valence force field for the $N_3—H_1\cdots O_9$ hydrogen bond. Optical measurements on CMH have been made by Kugel et al. (1979). These were interpreted in terms of a force model in which specific inter- and intramolecular interactions were represented by axially-symmetric force constants (Martel et al., 1977). Inelastic neutron-scattering measurements of some of the intermolecular mode dispersion curves have also been made for 1-MT (Martel and Powell, 1976) and CMH (Martel et al., 1977). Some of these results were also analyzed in terms of the same force model.

The similarity in the molecular ring structures of thymine and cytosine and the similar crystalline layer structure of 1-MT and CMH suggests that many of the intermolecular forces will be similar in these complexes. This approach was used in the analysis of the inelastic neutron scattering results (Martel et al., 1977). In the present paper we also exploit these similarities by assuming that corresponding nonbonded interactions are represented by the same interatomic potentials in both solids, and that differences in the dynamics of the two

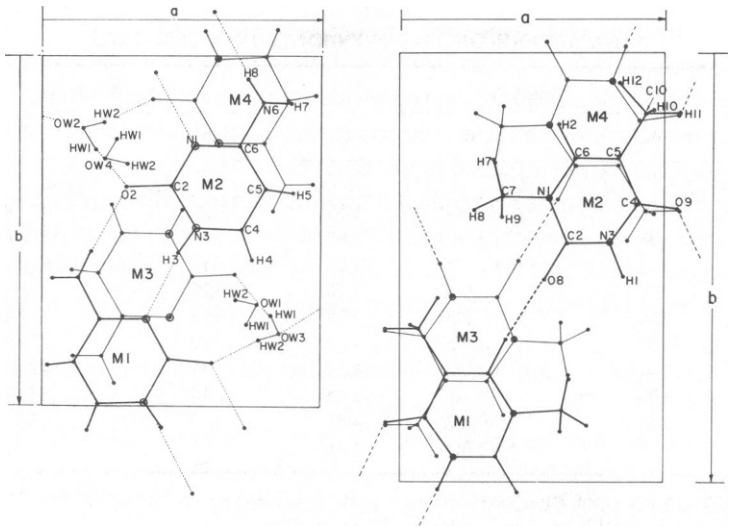

FIGURE 1 Projections of the unit cells of CMH (left) and 1-MT (right) on to the a-b plane. In both projections the molecules M1 and M2 lie in planes ~3.4 Å above those containing molecules M3 and M4. For CMH the four interplanar water molecules are represented as chevrons with labels OW_i at their apices. Hydrogen bonds are shown by the dotted (CMH) and dashed (1-MT) lines.

complexes are due to the different hydrogen bonding systems. We attempt to determine the hydrogen-bond potentials by analysis of the optical measurements at Γ. We assume that all nonbonded interactions can be represented by Buckingham pair potentials of the form

$$V(r_{ij}) = -\frac{A_{ij}}{r_{ij}^6} + B_{ij} \exp(-C_{ij} r_{ij}), \tag{1}$$

where r_{ij} is the interatomic separation of atoms i and j and A_{ij}, B_{ij} and C_{ij} are constants of this potential for atom pair i and j. We assume rigid molecules, i.e., that intramolecular forces are much stronger than intermolecular forces (see Dolling et al., 1973), we then represent the hydrogen bond interactions X—H---Y by Buckingham potentials between atoms H and Y only. In 1-MT, the two methyl groups in each molecule are each treated as single carbon atoms for the purposes of calculating the interatomic potentials.

Values for the constants of nonbonded Buckingham potentials applicable to heterocyclic molecules have been proposed by Kitaigorodskii et al. (1969), by Mirskaya and Nauchitel' (1972), by Caillet and Claverie (1975), and by Dashevskii et al. (1966), whereas Scott and Scheraga (1965) have proposed an approximate method for deriving these constants.

Methods for estimating the constants in hydrogen-bond potentials have been suggested by Poland and Scheraga (1967) and by Caillet and Claverie (1975). We have used the interpolation procedure of the latter authors to derive initial values for the hydrogen bond constants. The analytic form of the Buckingham potential results in strong correlations in B_{ij} and C_{ij} during any variational procedure. Consequently C_{ij} was held fixed at the value determined from the interpolation procedure whereas A_{ij} and B_{ij} were treated as adjustable

TABLE I
PARAMETERS OF THE NONBONDED POTENTIALS

Atom Pair	Model A			Model B		
	A	B	C	A	B	C
	(kcal · Å^6 mol^{-1})	(kcal · mol^{-1})	(Å^{-1})	(kcal · Å^6 mol^{-1})	(kcal · mol^{-1})	(Å^{-1})
C—C	358	42,000	3.58	421	47,000	3.49
C—N	308	42,640	3.68	367	55,500	3.67
C—O	313	57,100	3.85	349	63,900	3.79
N—N	259	42,000	3.78	320	65,500	3.86
N—O	256	57,200	3.98	304	75,400	3.99
O—O	259	77,000	4.18	289	87,000	4.12
C—H	154	42,000	4.12	131	47,000	4.24
N—H	109	36,200	4.25	114	55,500	4.46
O—H	106	49,200	4.50	109	63,900	4.60
H—H	57	42,000	4.86	41	47,000	5.15

The values for model A are from Kitaigorodskii et al. (1969), Mirskaya and Nauchitel' (1972) and Kirin et al. (1975), whereas those for model B are from Caillet and Claverie (1975).

parameters. In 1-MT there are two independent hydrogen bonds whereas in CMH there are five such interactions. The values for the hydrogen-bond parameters are expected to depend on the potentials assumed for the nonbonded interactions. To test this dependence we have carried out the calculations for two sets of nonbonded potentials. In model A we use the parameter values of Kitaigorodskii et al. (1969) and Mirskaya and Nauchitel' (1972), while in model B we use the parameter values derived from Caillet and Claverie (1975). Both sets of values are given in Table I for reference, and were held constant throughout the calculations. In the calculations, interactions with interatomic separations up to 8 Å were included for 1-MT and up to 6 Å for CMH. The shorter range for CMH was adopted to economize on computing time, but test calculations with the interaction range increased to 8 Å showed the calculated frequencies changed by <5%.

Kirin et al. (1975) have measured the frequencies of six A_g and five of the six B_g intermolecular modes in 1-MT by Raman scattering methods. The frequencies of the *ungerade* modes derived from their infrared (IR) measurements appear to be more uncertain, and there are discrepancies between these measurements and the data of Harada and Lord (1970). Consequently the four adjustable parameters for 1-MT were least squares fitted to the 11 experimental *gerade* frequencies. For CMH, the frequencies of 6 of the 12 A_g and 6 of the 12 B_g modes have been measured by Raman scattering (Kugel et al., 1979) but only 4 of the 21 *ungerade* modes were observed by IR methods. We have assumed the observed *gerade* modes to be the six lowest frequency A_g and B_g modes, respectively. Because we utilized only 12 frequencies and there are 10 adjustable parameters, a search was made throughout parameter space to find values that gave the minimum residual.

For both 1-MT and CMH the experimental polarization analysis appears to be imperfect and certain modes are observed in more than one polarization geometry. Consequently, the assignment of the observed peaks into A_g or B_g symmetry representations is ambiguous. We have used the classification scheme proposed by the original authors (Kirin et al., 1975; Kugel et al., 1979).

TABLE II

COMPARISON OF THE OBSERVED AND FITTED GERADE INTERMOLECULAR FREQUENCIES AT Γ IN 1-MT

Mode	Observed frequencies		Fitted frequencies	
	K	HL	Model A	Model B
	(units of cm^{-1})	*(units of cm^{-1})*	*(units of cm^{-1})*	*(units of cm^{-1})*
A_g	104	106	110	101
	81		75	76
	72		72	68
	61		52	62
	42		30	35
	28		19	22
B_g	108	106	115	116
	104	73	83	96
	72	61	75	80
			72	67
	44		46	56
			40	49
A_u		79	75	92
		56	57	68
	94	42	49	56
	80		44	46
	69		21	25
B_u	56	96	70	83
	~40	69	66	75
	~30	56	53	62
			36	44

The *ungerade* frequencies given in the column headed "fitted" are calculated from the best potential parameters. The designations K and HL for observed frequencies refer to Kirin et al. (1975) and Harada and Lord (1970), respectively.

RESULTS

1-MT

The results of fitting model A to the experimental A_g and B_g frequencies of 1-MT are shown in Table II, and the "best fit" parameters for the two hydrogen bonds are given in Table III. The fit is marginally better than that of model II of Kirin et al. (1975), but poorer than that of model I of the same authors. The largest discrepancies occur for the two lowest frequency A_g

TABLE III

THE FITTED POTENTIAL PARAMETERS FOR THE HYDROGEN BONDS IN 1-MT

Hydrogen bond X—H---Y	H---Y distance	Model A			Model B		
		A	B	C	A	B	C
	Å						
N_3—H_1---O_9	1.809	418 ± 40	68.7 ± 6.3	5.14	284 ± 49	45.0 ± 8.7	5.14
C_6—H_2---O_8	2.045	668 ± 43	118.9 ± 11.6	5.05	942 ± 259	177.4 ± 52.0	5.05

The units for A and C are as in Table 1 and the unit for B is 10^3 kcal · mol^{-1}.

modes and the second highest frequency B_g mode. In all these cases, the fitted frequencies are lower than those observed. However, the overall frequency range is calculated to be rather wider than is observed. In Table II, the calculated and experimental A_u and B_u frequencies are also compared. In view of the discrepancies between the two sets of experimental results, little can be deduced from the comparison. An unambiguous set of experimental *ungerade* frequencies is clearly required. The calculated potential energy, V, of a 1-MT molecule is -38.9 kcal · mol^{-1}. The N_3—H_1---O_9 bonds contribute 29% of this potential energy whereas the C_6—H_2---O_8 bonds contribute 27% of the total. The sublimation energy with which the quantity $\frac{1}{2}V$ might be compared has not been measured. The hydrogen-bond potentials are shown in Fig. 2.

Although there are no pure translational or pure librational intermolecular modes, most modes are predominantly one or the other in character. Only the lowest frequency A_u and the second lowest A_g modes show significant mixing of the two types of displacement. The highest frequency A_g and B_g modes both correspond to stretching of the N_3—H_1---O_9 hydrogen bonds, and the lowest frequency B_u mode involves a torsional motion about the same bonds. The highest frequency A_u mode is predominantly a translation perpendicular to the layer plane. The highest frequency B_u mode is an out-of-plane libration about an axis perpendicular to the dimer hydrogen bonds. There is no mode in which the dominant displacement is a libration of the molecule in its own plane. If the dimer hydrogen bonds are removed then all frequencies decrease, although not uniformly, and the modes tend to become more mixed in character. The highest frequency A_g and B_g modes show some of the largest frequency changes but their eigenvectors are largely unaffected. The lower frequency *gerade* modes show significant changes in eigenvector. The *ungerade* modes show less change in general, but the lowest A_u mode has a large decrease in frequency. If the C_6—H_2---O_8 bonds are removed, then all B_u modes are strongly affected, but the largest frequency change is shown by the lowest B_g mode whose frequency decreases by ~65%. The lowest frequency modes in the other symmetries are also affected, but the magnitude of the effect decreases for higher frequency modes.

The result of fitting model B to the observed A_g and B_g frequencies is also shown in Table II and the best-fit parameters for the hydrogen bonds are given in Table III. The fit is rather better than that of model A but still slightly poorer than that of model I of Kirin et al. (1975). There are no excessively large discrepancies between the fitted and observed frequencies as there were for model A, but the two lowest A_g modes and the second highest B_g mode are still calculated to be too low. The frequencies of the *ungerade* modes calculated from this model are uniformly higher than those of model A. The calculated potential energy, V, of a molecule is -39.8 kcal · mol^{-1}, very similar to that of model A, but the N_3—H_1---O_9 bonds contribute only 20% of this energy while the C_6—H_2---O_8 bonds contribute 36% of the total. The fitted potentials are also shown in Fig. 2.

The eigenvectors of the A_g modes are very similar in the two models, but there are significant differences for several other modes. More modes are of mixed translational-librational character in model B. The highest frequency B_u mode and the second highest frequency B_g and A_u modes all change from an almost pure librational character in model A to a totally mixed character in model B, whereas three other modes (the second lowest B_u and the middle two A_u modes) change character completely from one model to the other.

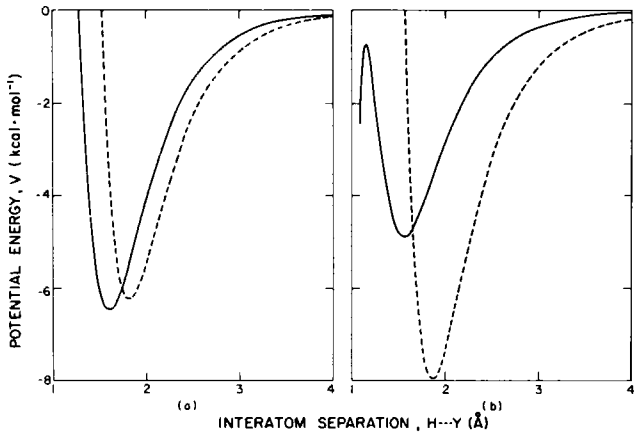

FIGURE 2 The fitted hydrogen bond potentials in 1-MT, *a* refers to model A and *b* refers to model B. —, N_3—H_1···O_9 potential; ---, C_6—H_2···O_8 potential.

CMH

The results of varying the parameters of model A to minimize the residuals for the 12 A_g and B_g experimental frequencies of CMH are shown in Table IV, and the parameters of the five hydrogen bonds are given in Table V. The calculated frequencies of the lowest A_u and B_u modes are also compared with the (arbitrarily assigned) observed values in Table IV. The calculated frequencies are in poor agreement with those observed; the former are ~35% too low. The discrepancies for the A_g modes are significantly greater than those for the B_g modes. None of the six lowest modes in each symmetry species show significant water motion, but the cytosine motions in all modes are rather complex and none have simple displacements. There is a more mixed translational-librational character than in 1-MT. An unexpected result is that none of the six higher frequency modes in each symmetry species show a dominant water motion. This contrasts with the model of Kugel et al. (1979). The higher frequency modes in each species do have a significant water component, but even these have a large cytosine motion. The calculated potential energy, V, of a cytosine molecule is -41.0 kcal · mol^{-1} and of a water molecule is -13.62 kcal · mol^{-1}, to which the hydrogen bonds contribute 46 and 64%, respectively. The sublimation energy of CMH has not been measured.

If the three hydrogen bonds to the water molecule are significantly reduced in magnitude, the lower A_g, B_g, and A_u modes are reduced in frequency; the effect is smaller for the higher frequency modes. The B_u modes are hardly affected by this change. However, many of the modes of all representations show significant changes in their eigenvectors. A general tendency is for all modes to have rather less-mixed character.

The results obtained for CMH with model B are very similar to those obtained with model A. The agreement with the experimental frequencies is slightly better with model B, but the calculated frequencies are still ~33% too low. The discrepancies are again worse for the A_g modes and the comparison is shown in Table IV. The proportion of cytosine or water motion and the proportion of translational or librational character is very similar for the two models with rather few modes showing significant differences. The calculated potential of cytosine is

TABLE IV

COMPARISON OF THE LOWEST OBSERVED AND "CALCULATED" INTERMOLECULAR FREQUENCIES OF EACH SYMMETRY SPECIES AT Γ IN CMH

Mode	Observed frequencies	Calculated frequencies	
		Model A	Model B
	(units of cm^{-1})	*(units of cm^{-1})*	*(units of cm^{-1})*
A_g	55	34	34
	71	38	39
	81	41	42
	93	57	59
	122	64	69
	170	104	110
B_g	57	32	35
	71	59	63
	89	68	70
	108	78	82
	122	86	89
	138	102	103
A_u		54	55
		59	59
		62	65
	72	75	83
	102	98	101
B_u		37	44
		58	59
	88	92	95
	95	95	100

The observed frequencies are from Kugel et al. (1979). The observed *ungerade* frequencies are arbitrarily assigned to the nearest calculated frequencies.

-42.68 kcal · mol^{-1} and of water is -13.78 kcal · mol^{-1}, with the hydrogen bonds contributing 48 and 66% respectively. The hydrogen-bond potentials are shown in Fig. 3. It is interesting to note that for both models the potentials for the two O_w—H_w---O_2 bonds are found to be almost identical although this requirement was not imposed in either case.

The calculated frequencies given in Table IV are uniformly higher for model B, but this feature does not persist for the highest frequency modes in any of the symmetry species. For

TABLE V

THE POTENTIAL PARAMETERS OF THE HYDROGEN BONDS IN CMH

Hydrogen bond X—H---Y	H---Y distance	Model A			Model B		
		A	B	C	A	B	C
N_3—H_3---N_1	2.086	397	54,000	4.85	426	55,125	4.85
N_6—H_6---O_2	2.121	380	65,000	4.98	420	74,500	4.98
N_6—H_7---O_w	2.166	485	81,000	4.91	418	74,250	4.91
O_w—H_{1w}---O_2	2.018	367	70,000	5.08	411	78,500	5.08
O_w—H_{2w}---O_2	1.989	360	73,000	5.11	419	84,500	5.11

The units for A, B, and C are as in Table I.

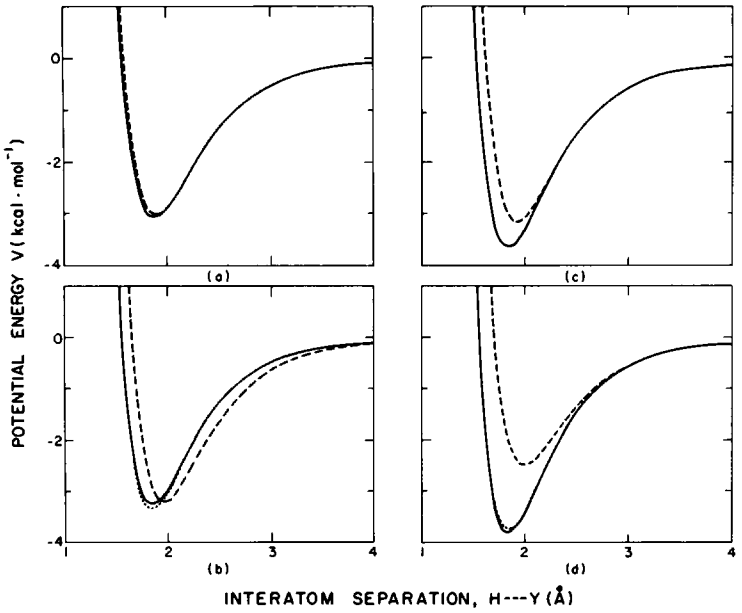

FIGURE 3 The calculated hydrogen bond potentials in CMH. *a* and *b* refer to model A, and *c* and *d* to model B. In *a* and *c* — represents the N_3—H_3---N_1 potential and --- represents the N_6—H_6---O_2 potential. In *b* and *d*, — represents the O_w—H_{2w}---O_2 potential, · · · · represents the O_w—H_{1w}---O_2 potential, and --- represents the N_6—H_7---O_w potential.

model A the highest intermolecular frequency is that of an A_g mode at 345 cm^{-1} and the frequency of the highest mode for each symmetry is >334 cm^{-1}. For model B, however, the highest intermolecular mode is at 294 cm^{-1} (also an A_g mode), whereas the highest frequency for each symmetry is >267 cm^{-1}. For all symmetries in both models there is a significant frequency gap (~67 cm^{-1}) between the three highest frequency modes and the remaining modes. The three highest frequency modes show the largest water displacement and are the only modes that have a nonzero water-libration component. The frequencies calculated for these "water" modes may be compared with observed frequencies of ~300 cm^{-1} and ~567 cm^{-1} (Renker, 1973) for translational and librational modes, respectively, of water molecules in ice.

DISCUSSION

In the case of 1-MT the representation of the hydrogen bonds (both of which are almost linear) by a simple Buckingham potential leads to satisfactory agreement with the experimental *gerade* frequencies. The fitted potentials for the two bonds in model A (Fig. 1 *a*) appear to be reasonable, although the depth of the potential for the C_6—H_2---O_8 bond is perhaps greater than might be expected for a "weak" hydrogen bond. Despite the better overall fit to the *gerade* frequencies the potentials of model B appear to be rather less reasonable (see Fig. 2 *b*). The C_6—H_2---O_8 potential has a very similar shape to that of Fig. 2 *a*, but the depth of the potential in Fig. 2 *b* is significantly greater. The N_3—H_1---O_9 potential in Fig. 2 *b* has a minimum (at an interatom separation of ~1.6 Å) similar to that of the corresponding

potential in Fig. 2 *a*. In Fig. 2 *b*, however, the potential becomes attractive again at an interatom separation of ~1.2 Å, whereas the potential of Fig. 2 *a* does not show this feature. Because of its particular analytic form, the Buckingham potential will always become attractive as the interatom separation tends to zero. The parameters of the N_3—H_1---O_9 potential in model B, however, cause this to happen at a larger separation than would usually be expected.

The description of the lowest *gerade* frequencies in CMH by a similar representation of the hydrogen bonds is much poorer. For both models the calculated values are much too low. This is also a feature of the model used by Martel et al. (1977) and Kugel et al. (1979), although the calculated frequencies in that case are only ~26% too low. Corresponding hydrogen-bond potentials for the two models of CMH are in much better agreement with each other than is the case for 1-MT. The calculated frequencies of the six lowest modes of each symmetry in CMH have a very similar range to those in 1-MT. If the water molecule and all the bonds to it are "removed" then the resulting (hypothetical) crystal structure is very similar to that of 1-MT. The frequency range remains largely unchanged in the "dehydrated" CMH, although all calculated frequencies decrease, and the character of the modes (i.e., translational or librational) becomes similar for dehydrated CMH and 1-MT. This suggests that for the 24 low-frequency modes in CMH (in which there is little water displacement), the water molecule simply acts as a source of additional bonding in the structure. The similarity in the calculated frequencies for 1-MT and CMH then follows from the similarity of the two crystal and molecular structures. However, since the calculated frequencies in CMH are, in reality, much too low, this suggests that some component of the interatomic interactions has been neglected. This component is either important for CMH but not for 1-MT, or can be simulated by the hydrogen-bond parameters in 1-MT but cannot be adequately simulated in CMH. The present calculations neglect contributions due to the polarizibility of the molecules and their electrostatic charge distribution. Effects of polarisibility are expected to be small for both 1-MT and CMH, but the electrostatic charge distribution of the water molecule in CMH has no equivalent in 1-MT. Consequently, neglect of electrostatic interactions is expected to be more serious in CMH. The present calculations suggest that interactions that result from the charge distributions of the cytosine and 1-MT molecules are included in the nonbonded and hydrogen-bond parameter in some sense, but the interactions from the charge distribution of the water molecule in CMH apparently cannot be included. It is therefore the neglect of these interactions that is probably responsible for the large discrepancies between the observed and calculated frequencies in CMH.

Kugel et al. (1979) measured the frequency shifts of the A_g and B_g modes produced by partial deuteration of CMH and we have calculated the corresponding shifts using the parameters of our models. The deuterated specimen was determined by mass spectrographic analysis to contain 67% $C_4H_2D_3N_3O$ and 47% D_2O. It is expected that the nonexchangeable hydrogens are at the H_4 and H_5 sites in the cytosine ring and the calculations were made on this assumption. The results are shown in Table VI. As might be expected the shifts calculated for the two models are rather similar, although differences in detail exist. Their overall magnitude is in good agreement with those observed, but the shifts calculated for individual modes show discrepancies in the experimental results. This indicates that specific mode eigenvectors derived from the present models are inadequate.

TABLE VI

COMPARISON OF THE OBSERVED AND CALCULATED FREQUENCY SHIFTS ($\Delta\nu$) FOR THE A_g AND B_g MODES IN CMH ON PARTIAL DEUTERATION

Mode	$\Delta\nu$ observed	Model A		Model B	
		ν_H calculated	$\Delta\nu$ calculated	ν_H calculated	$\Delta\nu$ calculated
	%	cm^{-1}	%	cm^{-1}	%
A_g	−0.9	34	−1.7	34	−2.0
	−1.4	38	−1.4	39	−0.9
	−1.6	41	−1.9	42	−2.2
	−1.6	57	−1.0	59	−0.9
	−1.9	64	−1.9	69	−1.7
	−2.7	104	−1.4	110	−1.8
B_g	−0.9	32	−0.9	35	−0.9
	−1.4	59	−1.9	63	−1.1
	−0.6	68	−1.2	70	−2.5
	−0.7	78	−2.1	82	−1.9
	−1.9	86	−0.9	89	−0.8
	−1.2	102	−0.5	103	−1.7

$\Delta\nu \equiv (\nu_D - \nu_H)/\nu_H$, where $\nu_H(\nu_D)$ are the frequencies in hydrogenous (deuterated) CMH.

The assumption of "rigid molecules" is probably not very well satisfied for these molecules and an interaction between the internal and external modes should be included. Theoretical formalisms exist to describe the inclusion of such an interaction (Pawley and Cyvin, 1970; Piseri, 1973). The effects will be largest for the highest frequency intermolecular and the lowest frequency intramolecular modes and the tendency will be to lower the rigid-molecule intermolecular frequencies. However, it is unlikely that neglecting this interaction caused the discrepancies between the present calculations and the observed frequencies.

In the present calculations each hydrogen bond potential has been treated as independent with a parameter, C_{ij} (see Eq. 1 and Tables III and V) determined by the interpolation procedure of Caillet and Claverie (1975). The potential is not determined directly, but only in terms of its first ($\partial V/\partial r$) and second ($\partial^2 V/\partial r^2$) derivatives at the appropriate interatomic separation (H---Y). In practice, this does not determine the potential very specifically and allows considerable ambiguity in the constants of the potential. In Table VII the values for ($\partial V/\partial r$) and ($\partial^2 V/\partial r^2$), determined for the two models in the present calculations, are compared with the corresponding values in the model calculations of Martel et al. (1977) and Kugel et al. (1979), which include a limited number of specific interactions. In the present calculations the derivatives refer to the H---Y interaction, whereas in this alternative model they refer to the X—Y interaction. Knowing the sublimation energy would help in specifying the potentials. For 1-MT and CMH, however, the total calculated potential of a molecule (V) has similar values for models A and B. Thus, the variation of this potential to fit an experimental sublimation energy might tend to scale the potentials, rather than define their specific shape more precisely.

The values of the derivatives (which are related to interatomic force constants) given in Table VII show that for CMH the hydrogen bonding to the water molecule contributes a

TABLE VII

COMPARISON OF THE FIRST AND SECOND DERIVATIVES OF THE HYDROGEN BOND POTENTIALS OF THE PRESENT CALCULATIONS AND THOSE USED BY MARTEL ET AL. (1977) AND KUGEL ET AL. (1979)

	Hydrogen bond X—H---Y	Model A		Model B		Martel et al. (1977) and Kugel et al. (1979)	
		$\frac{\partial V}{\partial r}$	$\frac{\partial^2 V}{\partial r^2}$	$\frac{\partial V}{\partial r}$	$\frac{\partial^2 V}{\partial r^2}$	$\frac{\partial V}{\partial r}$	$\frac{\partial^2 V}{\partial r^2}$
		$10^{-10}N$	$N \cdot m^{-1}$	$10^{-10}N$	$N \cdot m^{-1}$	$10^{-10}N$	$N \cdot m^{-1}$
1-MT	N_3—H_1---O_9	5.01	9.13	3.96	3.37	−0.31	6.8
	C_6—H_2---O_8	4.97	5.18	5.89	13.00	−0.09	1.9
CMH	N_3—H_3---N_1	2.28	3.15	2.83	1.54	−0.32	6.8
	N_6—H_6---O_2	2.39	1.94	2.40	3.33	−0.09	1.9
	N_6—H_7---O_w	2.39	3.22	1.70	4.53	2.97	9
	O_w—H_{1w}---O_2	2.50	5.23	2.79	5.93	2.79	9
	O_w—H_{2w}---O_2	2.20	8.07	2.62	9.07	2.85	9

significant fraction of the total intermolecular force. This suggests that hydration interactions will be very important in model calculations of biomolecular dynamics. The observation that different configurations of DNA form in different aqueous environments is further evidence of the importance of hydration interactions.

A definitive determination of the hydrogen-bond potentials requires more experimental data on enough molecular solids for the assumption of transferability to be effectively utilized. Instead of each bond being treated individually, the same potential would then be assumed for similar bonds independent of their length and of the particular molecular solid in which they occur. Calculations analogous to the present ones would then determine $\partial V/\partial r$ and $\partial^2 V/\partial r^2$ at several interatomic distances (H_i---Y_i) and so define the potential much more precisely. The similarity obtained for the O_w—H_{1w}---O_2 and O_w—H_{2w}---O_2 hydrogen bond potentials in CMH gives support to this assumption of transferability. This approach means that experimental intermolecular frequencies must be measured for several more DNA base complexes and we hope that such data will become available.

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REFERENCES

Caillet, J., and P. Claverie. 1975. Theoretical evaluation of the intermolecular energy of a crystal: application to the analysis of crystal geometry. *Acta Crystallogr. Sect. A.* 31: 448–461

Dashevskii, V. G., Yu. T. Struchkov, and Z. A. Akopyan. 1966. Conformation of overloaded aromatic nitrocompounds. *J. Struct. Chem. (U. S. S. R.).* 7: 555–561

Dolling, G., G. S. Pawley, and B. M. Powell. 1973. Interatomic forces in hexamethylenetetramine. *Proc. R. Soc. (Lond.) A.* 333: 363–384.

Eyster, J. M., and E. W. Prohofsky. 1974*a*. Lattice vibrational modes of poly(rU) and poly(rA). *Biopolymers.* 13: 2505–2526.

Eyster, J. M., and E. W. Prohofsky. 1974*b*. Lattice vibrational modes of poly(rU) · poly(rA). A coupled single-helical approach. *Biopolymers.* 13:2527–2543.

Eyster, J. M., and E. W. Prohofsky. 1977. Soft modes and the structure of the DNA double helix. *Phys. Rev. Lett.* 38: 371–373.

Harada, I., and R. C. Lord. 1970. Low frequency infrared and Raman spectra of some adenine and uracil crystals. *Spectrochim. Acta Part A. Mol. Spectrosc.* 26: 2305–2318.

Hoogsteen, K. 1963. The crystal structure of 1-methylthymine. *Acta Crystallogr.* 16: 28–38.

Jeffrey, G. A., and Y. Kinoshita. 1963. The crystal structure of cytosine monohydrate. *Acta Crystallogr. Sect. A.* 16: 20–28.

Kirin, D., L. Colombo, K. Furić, and W. Meier. 1975. Low frequency vibrational spectrum of the 1-methylthymine single crystal. *Spectrochim. Acta Part A Mol. Spectrosc.* 31A: 1721–1727.

Kitaigorodskii, A. I., K. V. Mirskaya, and V. V. Nauchitel'. 1969. Interactions of the C—O and O—O atoms in CO_2 crystals. *Sov. Phys. Crystallogr.* 14: 769–771.

Kugel, G. E., X. Gerbaux, C. Carabatos, P. Martel, and B. M. Powell. 1979. Low frequency vibrational Raman and i.r. spectrum of crystalline cytosine monohydrate. *Spectrochim. Acta Sect. A. Mol. Spectrosc.* 35A: 1155–1163.

Kvick, A., T. F. Koetzle, and R. Thomas. 1974. Hydrogen bond studies. 89*. A neutron diffraction study of hydrogen bonding in 1-methylthymine. *J. Chem. Phys.* 61: 2711–2719.

Lu, K-C., E. W. Prohofsky, and L. L. Van Zandt. 1977. Vibrational modes of A-DNA, B-DNA, and A-RNA backbones: an application of a green function refinement procedure. *Biopolymers.* 16: 2491–2506.

Lu, K-C., L. L. Van Zandt, and E. W. Prohofsky. 1979. Displacements of backbone vibrational modes of A-DNA and B-DNA. *Biophys. J.* 28: 27–32.

Maret, G., R. Oldenbourg, G. Winterling, K. Dransfeld, and A. Rupprecht. 1979. Velocity of high frequency sound waves in oriented DNA fibers and films determined by Brillouin scattering. *Colloid Polymer Science.* 257: 1017–1020.

Martel, P., and B. M. Powell. 1976. Measurement of acoustic modes of vibration in 1-methylthymine by neutron scattering. *Chem. Phys. Lett.* 39: 339–340.

Martel, P., B. M. Powell, and L. A. Vinhas. 1977. The lattice dynamics of crystalline DNA pyrimidines. *In* Proceedings of the international Conference on Lattice Dynamics. M. Balkanski, editor. Flammarion Sciences, Paris. 494–497.

McClure, R. I., and B. M. Craven. 1973. New investigations of cytosine and its monohydrate. *Acta Crystallogr. Sect. B Struct. Crystallogr. Cryst. Chem.* B29: 1234–1238.

Mirskaya, K. V., and V. V. Nauchitel'. 1972. Determination of the parameters of the non-valence interaction curve of nitrogen atoms. *Sov. Phy. Crystallogr.* 17: 56–59.

Momany, F. A., L. M. Carruthers, R. F. McGuire, and H. A. Scheraga. 1974. Intermolecular potentials from crystal data. III. Determination of empirical potentials and application to the packing configurations and lattice energies in crystals of hydrocarbons, carboxylic acids, amines and amides. *J. Phys. Chem.* 78: 1595–1621.

Pawley, G. S., and S. J. Cyvin. 1970. Lattice vibrations in crystals with deformable molecules: A calculation for naphthalene. *J. Chem. Phys.* 52: 4073–4077.

Piseri, L. 1973. On the separation of internal and external vibrations in molecular crystals. *J. Phys. C. Solid State.* 6: 1521–1529.

Poland, D., and H. A. Scheraga. 1967. Energy parameters in polypeptides. I. Charge distributions and the hydrogen bond. *Biochemistry.* 6: 3791–3800.

Renker, B. 1973. Lattice dynamics of hexagonal ice. *In* Physics and Chemistry of Ice. E. Whalley, S. J. Jones, and L. W. Gold, editors. Royal Society of Canada, Ottawa. 82–86.

Scott, R. A., and H. A. Scheraga. 1965. Method for calculating internal rotation barriers. *J. Chem. Phys.* 42: 2209–2215.