

Molecular Dynamics Simulation of Sucrose in Aqueous and Dimethyl Sulfoxide Solution

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Molecular dynamics simulations have been carried out to study the motion of a single sucrose molecule in two solvents, water and dimethyl sulfoxide at 300 K. Starting from a crystal structure of sucrose, no major conformational transitions are observed for the dihedral angles of the glycosidic linkage, nor are they observed for any of the hydroxymethyl groups in either of the solutions during 200 ps, the duration of the production part in both simulations. Hydroxyl groups usually show frequent transitions, except for those involved in hydrogen bonding between the two sugar residues in sucrose. Inter-residue hydrogen bonding is observed between O5g and H'6f for more than half of the simulation time and between O1f and H'2g for about half of the simulation time both in water and in dimethyl sulfoxide. Radial distribution functions were calculated between oxygens or hydroxyl protons of the solute and solvent oxygen atoms. Radial distribution functions typical of hydrogen bonding to solvent are observed for the hydroxyl groups of sucrose except for those involved in inter-residue hydrogen bonding, where coordination numbers are reduced. Translational diffusion constants were calculated from the simulations and were for sucrose $1.2 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ in water and $0.13 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ in dimethyl sulfoxide.

The structure and conformation of sucrose has been studied a great deal. With the advent of molecular dynamics the study of flexibility and dynamical processes of molecules have gained additional momentum. The crystal structure¹ has been known for a long time. Sucrose has been studied using X-ray diffraction,² laser Raman spectroscopy,^{3,4} optical rotation,⁵ rigid residue modelling and NMR spectroscopy,^{6,7} molecular mechanics,⁸ NMR spectroscopy^{9–21} *per se* and molecular dynamics studies *in vacuo*.²² Recently, a molecular dynamics simulation was performed on nystose,²³ which contains sucrose as a building block. Computer modelling methods predict one or more low-energy conformers for sucrose in the region close to the crystal structure. In the crystal, intramolecular hydrogen bonding is observed between the hydroxyl proton of O2 in the glucose residue and O1 in the fructose residue, as well as between the hydroxyl proton of O6 in the fructose residue and O5 in the glucose residue, but other hydrogen bonding patterns have also been put forward, like from the hydroxyl proton of O3 in the fructose residue to O2 in the glucose residue, depending on conditions. The issue of whether hydrogen bonding plays a key role in stabilizing certain conformations in sucrose and the flexibility of the molecule, especially over the gly-

cosidic linkage, has been extensively studied by NMR spectroscopy. Arguments have been put forward that intramolecular hydrogen bonds exist both in water and in dimethyl sulfoxide⁶ (DMSO), but also that if they exist, they should not be persistent in water.¹⁹

The inclusion of solvent in molecular dynamics studies compared to *in vacuo* simulations makes it possible to study the properties of sucrose in an environment where comparison can be made with a number of experimental observations. The interaction between solute and solvent and the way solvent possibly influences the properties of the solute can also be investigated. The drawback of solvent simulations is the large increase in computation time required. We report here molecular dynamics studies of sucrose in water and in DMSO.

Physical models and computational methods

We have used the standard NVE MD method²⁴ for the simulations. The simulation in both solutions is started by placing a single sucrose molecule, which had been energy-minimized from its crystal structure¹ using MM2,²⁵ at the center of a cubic simulation cell filled with 255 solvent molecules. Both the sucrose molecule and the solvent molecules are kept rigid in the beginning of the simu-

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lation. In this first equilibration period (20 ps) the simulation box is allowed to relax to a dimension corresponding to a normal density of water for the total system. In the next equilibration period of 50 ps the sucrose is allowed to become fully flexible. Finally, a complete MD simulation is carried out during 200 ps in each of the solvents. The solvent molecules are kept rigid even in the production period. The box lengths and temperatures for the simulations in water and in DMSO are 20.03 Å and 303 K, and 31.28 Å and 305 K, respectively.

The integration of the equations of motion for the rigid molecules are performed using the Leap-frog formulation²⁶ of the Verlet algorithm²⁷ for the linear motion and the quaternion-based leap-frog scheme by Fincham²⁸ for the rotational motion. The flexible molecule is treated with leap-frog displacements for the atomic positions. All bond constraints are employed by passing the coordinates through the SHAKE procedure.²⁹ The force field used for the sucrose non-bonded and bonded interactions is that of Homans.³⁰ Water molecules are furnished with TIP4P parameters³¹ and DMSO is modeled according to Rao and Singh.³² United atoms are used for the CH₃ groups of DMSO. Simple combination rules of Lorentz–Berthelot type are used for all the non-bonded cross-interactions. The long range Coulombic interactions are treated using the direct Ewald summation method. Lennard–Jones interactions were calculated using a spherical cut-off radius of half a box length. All the simulations are performed using a modified version of McMOLDYN computer simulation package³³ on a CONVEX C220 computer.

Nomenclature. The atoms of the two residues of sucrose are labelled by lower-case g and f for the glucose and fructose residues, respectively. Hydroxyl protons are marked by a prime. Torsion and bond angles are defined by:

$$\phi = \text{H1g-C1g-O1g-C2f}$$

$$\psi = \text{C1g-O1g-C2f-O5f}$$

$$\omega_{6g} = \text{O5g-C5g-C6g-O6g}$$

$$\omega_{1f} = \text{O5f-C2f-C1f-O1f}$$

$$\omega_{6f} = \text{O5f-C5f-C6f-O6f}$$

$$\tau = \text{C1g-O1g-C2f}$$

Torsion dihedrals of hydroxyl groups (χ) are defined by H'X–OX–CX–C(X-1), where X is an atomic position, except for the dihedral H'1f–O1f–C1f–C2f. Dihedral angles are 0° for the *cis* conformation and, when viewed along the central bond, a clockwise rotation of the far bond is defined as positive. Cremer–Pople parameters (CPP)³⁴ are described for the furanose ring by the phase angle ϕ_2 and the total puckering amplitude q_2 . The pyranose ring is described by a spherical polar set with the total puckering amplitude Q , the polar angle q and an azimuthal angle (not calculated, as q was close to zero). The

puckering amplitude is a measure of the displacement of the ring atoms from the mean plane. The phase angle ϕ_2 describes where the furanoid ring is on the envelope-twist pseudorotational itinerary.

Results and discussion

Sucrose conformation. The conformation of sucrose is described mainly by the dihedral angles ϕ and ψ , which determine the relative orientation of the two sugar residues in the molecule. The conformation of each sugar residue is described by the Cremer–Pople pucker parameters. The conformational changes occurring on energy minimization using MM2 on a single sucrose molecule having the crystal conformation were only minor. In the present simulations the MM2 energy-minimized structure was used as the starting conformation. The solute conformation after the equilibration period (Fig. 1) and during the production part of the simulation is described by a conformation close to that of the crystal structure, both in water and in DMSO. The dihedral angles ϕ and ψ have average values of $-2^\circ/-55^\circ$ and $-2^\circ/-58^\circ$ in water and in DMSO, respectively (Table 1). Measurement of the long-range ¹H, ¹³C coupling constant between H1g and C2f in both D₂O and in DMSO¹⁶ yielded values of 3.8 and 4.0 Hz for sucrose, respectively. Interpreting the magnitude of the coupling constant using a Karplus-type curve shows that the average conformation for the dihedral angle ϕ should be in the region $\pm 30-35^\circ$. The average conformation for the angle ϕ in the simulations is not in agreement with these experimental data. No transitions took place for the glycosidic dihedral angles, and the r.m.s. fluctuations were ca. 7°. It is not justified to draw conclusions about the rigidity of the system from the present simulation as no ϕ/ψ transitions took place, and the course of the simulation is short and

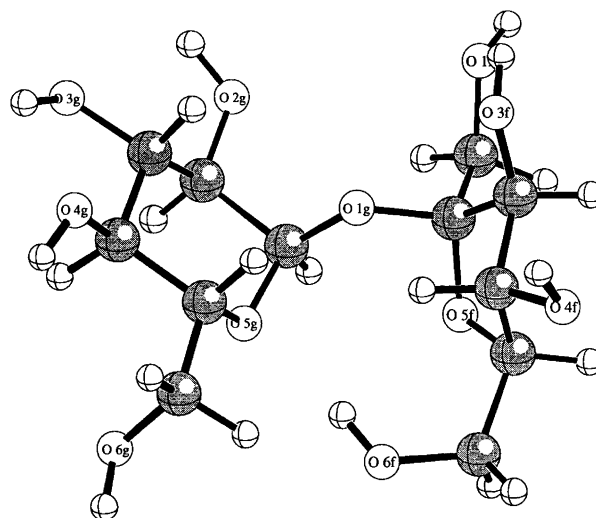


Fig. 1. Conformation of sucrose in water after the equilibration period.

Table 1. Initial geometries and averages over the MD simulations.^a

	MM2	Water		DMSO	
θ	5.10	6.4	(3.2)	6.3	(3.4)
Q	0.612	0.568	(0.029)	0.575	(0.030)
ϕ_2	265.2	268.0	(5.7)	267.2	(5.9)
q_2	0.346	0.512	(0.035)	0.508	(0.035)
τ	115.4	117.5	(2.9)	117.4	(3.1)
ϕ	-7.5	-2.0	(7.7)	-2.2	(7.6)
ψ	-43.6	-55.4	(6.3)	-57.9	(5.8)
$\omega 6g$	-55.1	-61.7	(6.5)	-61.4	(6.3)
$\omega 1f$	170.5	180.2	(5.6)	180.8	(5.7)
$\omega 6f$	-71.2	-60.7	(5.9)	-61.8	(6.3)
$\chi 2g$	100.2	-59.6	(15.7)	-53.5	(13.7)
$\chi 3g$	-99.2	-65.3	(29.2)	-59.4	(15.3)
$\chi 4g$	55.3	62.5	(22.1)	50.3	(23.1)
$\chi 6g$	86.3	182.4	(16.2)	36.5	(16.1)
$\chi 1f$	-76.7	53.7	(16.8)	54.5	(20.4)
$\chi 3f$	62.0	55.4	(30.7)	61.5	(16.5)
$\chi 4f$	130.5	66.8	(16.3)	175.4	(20.4)
$\chi 6f$	68.6	55.4	(12.6)	49.9	(13.3)

^aCPP parameters, glycosidic bond angle and dihedral angles. MM2 indicates the conformation minimized by molecular mechanics. The root mean-square of the fluctuations are given in parentheses.

of the same order of magnitude as the reorientational correlation time. The conformation of the glucose residue is the ⁴C₁ chair, as the CPP parameters are ca. 6° and 0.57 for q and Q , respectively. The fructose residue is described by a ⁴T₃ twist conformation, as the phase angle ϕ_2 is very close to 270°. In water the fructose residue of sucrose has been shown from ³J_{H,H} to be an average between the adjacent ⁴T₃ and ⁴E conformers.⁷ Other conformers close to these on the pseudorotational itinerary³⁵ have low barriers to interconversion³⁶ which make population of these conformers possible as seen in the MD simulations of sucrose *in vacuo*.²² The amplitude q_2 is larger, ca. 0.51, than for the crystal or MM2 energy-minimized structure. The r.m.s. fluctuations are low (Table 1), and no transitions were observed in the CPP. In the adiabatic potential energy map of sucrose⁸ three low-energy regions could be identified. In contrast to the present study the MD simulation of sucrose *in vacuo*²² showed a transition in ψ between two of these regions. There are three hydroxymethyl groups in sucrose with the corresponding dihedral angles $\omega 6g$, $\omega 1f$ and $\omega 6f$. Like the previously discussed dihedrals, they show no transitions during the course of the simulations. The dihedral angle $\omega 6g$ is in the *gg* (-60°) state using standard carbohydrate terminology. The hydroxymethyl dihedral angles $\omega 1f$ and $\omega 6f$ are described by *tg* (180°) and *gg* (-60°), respectively.

In contrast to the above, transitions occur for the hydroxyl groups as seen in Fig. 2. The behavior can be divided into two categories, *viz.* the hydroxyl groups involved in inter-residue hydrogen bonding (*vide infra*) and those that are not or to a minor extent. The hydroxyl groups involved in hydrogen bonding to the solvent show

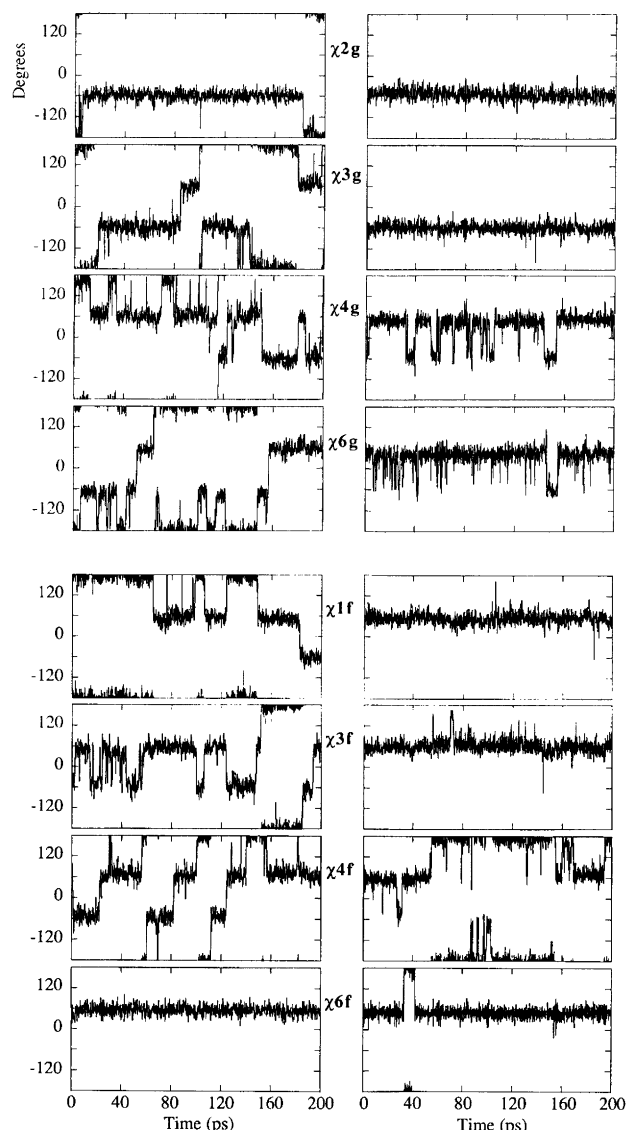


Fig. 2. Hydroxyl dihedral angles as a function of time. Left column: water simulation; right column: DMSO simulation.

more frequent transitions between their staggered conformers than those participating in inter-residue hydrogen bonding. A concerted transition is observed for the hydroxyl dihedral angles $\chi 2g$ and $\chi 1f$ in water around 180 ps. A series of cooperative transitions of the dihedral angles $\chi 1f$ and $\chi 3f$ begins after about 100 ps of the water simulation. Owing to the *tg* conformation of the dihedral $\omega 1f$, the pertinent hydroxyl groups can undergo hydrogen bonding through H' 1f and H' 2f (*vide infra*); this type of coupled transition takes place five times during the latter part of the simulation. In the DMSO simulation two transitions of $\chi 4g$, around 150 ps, are each followed by $\chi 6g$ transitions ca. 2 ps later.

Proton-proton distances. Non-exchangeable protons in molecules are often used for obtaining distance information by the nuclear Overhauser effect (NOE), although

hydroxyl protons of sugars can also be used in DMSO solution to obtain additional distance information to the usually scarce proton–proton interactions over the glycosidic linkage. In Table 2 selected proton–proton distances are shown. Each of the distances is very similar in both simulations. The r.m.s. fluctuations are ~ 0.1 – 0.3 Å. Two inter-residue distances < 3 Å are observed, i.e. H1g–H1f pro-*R* at an average distance in water of 2.18 Å and H5g–H4f at 2.67 Å. The H1g–H2g distance of 2.41 Å may be used as a reference in comparison of NOEs. Hervé du Penthoat *et al.*⁷ performed steady-state NOE measurements in which the NOE from H1g to H1f was 7%, to H4f 0.7% and to H2g 18%; additionally from H1f to H1g the NOE was 9.5%. On irradiation of H4f a weak NOE was observed to, *inter alia*, H1g (1.5%), which is just above 4 Å in the present simulations, but an NOE to H5g was not reported. The conformation in the present simulations is thus not supported to be present exclusively in solution as judged from the NOE data acquired by Hervé du Penthoat *et al.*⁷

Hydrogen bonding. In the present simulations inter-residue hydrogen bonding is observed; data are given in Table 3 and hydrogen-bond occurrences during the simulation are shown in Fig. 3. The hydrogen bonds are calculated using the criteria $O_{\text{solute}} \cdots O_{\text{water}} < 3.5$ Å and $O_{\text{solute}} \cdots H-O_{\text{water}}$ or $O-H_{\text{solute}} \cdots O_{\text{water}} > 135^\circ$. The same distance and angle criteria are also used for intra-sucrose hydrogen bonding. The hydrogen bond from H'6f to O5g is the most frequent one in both solvents. H'6f also acts as a donor to O1g for short periods of the simulations. The second pair involved in inter-residue hydrogen bonding is H'2g to O1f and to some extent the alternating H'1f to O2g in water, which occurs after 180 ps when transitions occur for χ 2g and χ 1f. This hydrogen-bonding pattern is made possible due to the *tg* conformation of the ω 1f dihedral angle.⁷ A difference between sucrose in two solvents is that inter-residue hydrogen bonds are occurring with a higher probability in DMSO solution. One hydrogen bond that occurs to a noticeable degree is the intra-residue H'1f to O3f and also H'3f to O1f in water. This is facilitated by the *tg* conformation of the ω 1f dihedral angle. Alternating χ 1f

and χ 3f transitions lead to intra-residue hydrogen bonds being formed and broken. In DMSO it is only the H'1f to O3f hydrogen bond that is being formed. Figure 4 depicts the two inter-residue hydrogen bonds that exist with greatest probability. As mentioned above, transitions of hydroxyl groups involved in inter-residue hydrogen bonds do not make frequent transitions. Comparison between Figs. 2 and 3 further shows this facts, being exemplified by χ 2g and χ 6f.

Radial distribution functions. Solvation can be investigated using atomic radial distribution functions³⁷ $g_{nm}(r)$ where the first index n refers to a solute atom and the second index refers to a solvent atom. Two kinds of radial distribution functions were studied (i) solute–oxygen to solvent–oxygen distributions represented by $g_{OO}(r)$ and (ii) solute–hydroxyl proton to solvent–oxygen distributions represented by $g_{HO}(r)$. The numbers of near neighbor water molecules from pair distribution functions for hydroxyl protons and hydroxyl oxygens to water oxygens were integrated out to 2.4 and 3.5 Å, respectively.

Radial distribution functions of some selected hydroxyl groups are shown in Fig. 5. The $g_{OO}(r)$ distributions in water show a first maximum around 2.6 Å, but the intensity and shape of the curve after the first maximum differ between the curves presented. The first sharp maximum at this distance is indicative of hydrogen bonding. Integration of $g_{OO}(r)$ out to the first minimum (Table 4) shows a higher coordination number for the primary O6g hydroxyl group than e.g. the primary hydroxyl groups of the fructose group, which are both involved in hydrogen bonding to the glucose residue. This is readily seen for the $g_{HO}(r)$ distribution for H'6f, which has inter-residue hydrogen bonding to O5g, and thus the maximum around 2.1 Å is not present. This is also the case for the DMSO simulation, where the H'6f–O5g hydrogen bond is present to an ever larger extent. The integral of the radial distribution function of H'6f to water oxygens is severely reduced. This is also the case for the H'6f hydrogen bonding to solvent, which occurs only to a small amount compared to the hydrogen bond of H'6g to solvent oxygens. A second maximum around 3.2 Å is clearly identified for the $g_{HO}(r)$ distributions in water due to the structure of the first coordination shell.³⁷ Hydrogen bonding to solvent and $g_{HO}(r)$ are also reduced for the other hydroxyl groups involved in inter-residue hydrogen-bonding, i.e. H'2g and H'1f, as well as for H'3f, which has an intra-residue hydrogen bond.

The hydroxyl groups act as both donors and acceptors for hydrogen bonding (Table 4). The total hydrogen bonding for each hydroxyl group, i.e. the sum of the hydroxyl oxygen as an acceptor and the hydroxyl hydrogen as a donor, is about half of its integrated $g_{OO}(r)$ value out to the first minimum at 3.5 Å for all hydroxyl groups in sucrose. For the hydroxyl groups that are mainly hydrogen bonding to solvent, the hydroxyl oxygen shows about twice as many hydrogen bonds as an acceptor compared to the hydroxyl hydrogen which acts as a donor. The

Table 2. Selected distances between non-exchangeable protons.^a

Atom pair	Distance/Å			
	Water		DMSO	
H1g–H1fpro- <i>R</i>	2.18	(0.17)	2.14	(0.16)
H1g–H1fpro- <i>S</i>	3.58	(0.14)	3.56	(0.14)
H1g–H3f	4.37	(0.25)	4.61	(0.12)
H1g–H4f	4.01	(0.16)	4.07	(0.14)
H1g–H6fpro- <i>R</i>	5.33	(0.21)	5.37	(0.18)
H1g–H6fpro- <i>S</i>	4.41	(0.26)	4.42	(0.23)
H1g–H2g	2.41	(0.11)	2.43	(0.11)
H5g–H4f	2.67	(0.22)	2.63	(0.21)

^aR.m.s. fluctuations in parentheses.

Table 3. Intra- and inter-residue hydrogen bonds of sucrose in water and in DMSO solution.^a

Acceptor	Donor	Probability (%)	$\langle O\cdots H \rangle / \text{\AA}$	$\langle O\cdots O \rangle / \text{\AA}$	$\langle O\cdots H-O \rangle / ^\circ$
Water					
O1g	H' 6f	2.6	2.6	3.4	143
O2g	H' 1f	5.5	2.1	2.9	147
O5g	H' 6f	65.0	2.2	2.8	147
O1f	H' 3f	7.4	2.0	2.8	141
O1f	H' 2g	44.3	2.0	2.8	141
O3f	H' 1f	10.8	2.1	2.9	141
DMSO					
O1g	H' 6f	8.3	2.5	3.4	144
O5g	H' 6f	81.4	2.1	3.0	151
O1f	H' 2g	67.8	2.0	2.9	150
O3f	H' 1f	29.6	2.0	2.8	142

^a $\langle \cdots \rangle$ indicates an average value over the simulation.

number of solute–solvent hydrogen bonds has been shown to be rather insensitive to small changes in the distance cutoff but very sensitive to the angular cutoff.³⁸ The somewhat arbitrary definition using a value of 135° , which is quite large, therefore reduces the number of possible hydrogen bonds. In a recent MD simulation of cellobiose in water³⁹ about two hydrogen bonds per hydroxyl group were observed when the integrated $g_{OO}(r)$

value was around 3 for the hydroxyl group. Integration of $g_{HO}(r)$ for sucrose out to the first minimum or calculation of hydrogen bonds from the hydroxyl hydrogen to solvent using the above criteria give essentially identical results for the hydroxyl hydrogens (Table 4). In DMSO the first maxima are found around 3.0 Å for $g_{OO}(r)$ distributions and 2.2 Å for $g_{HO}(r)$ distributions, respectively. The first maximum is well defined for the $g_{HO}(r)$ distributions pre-

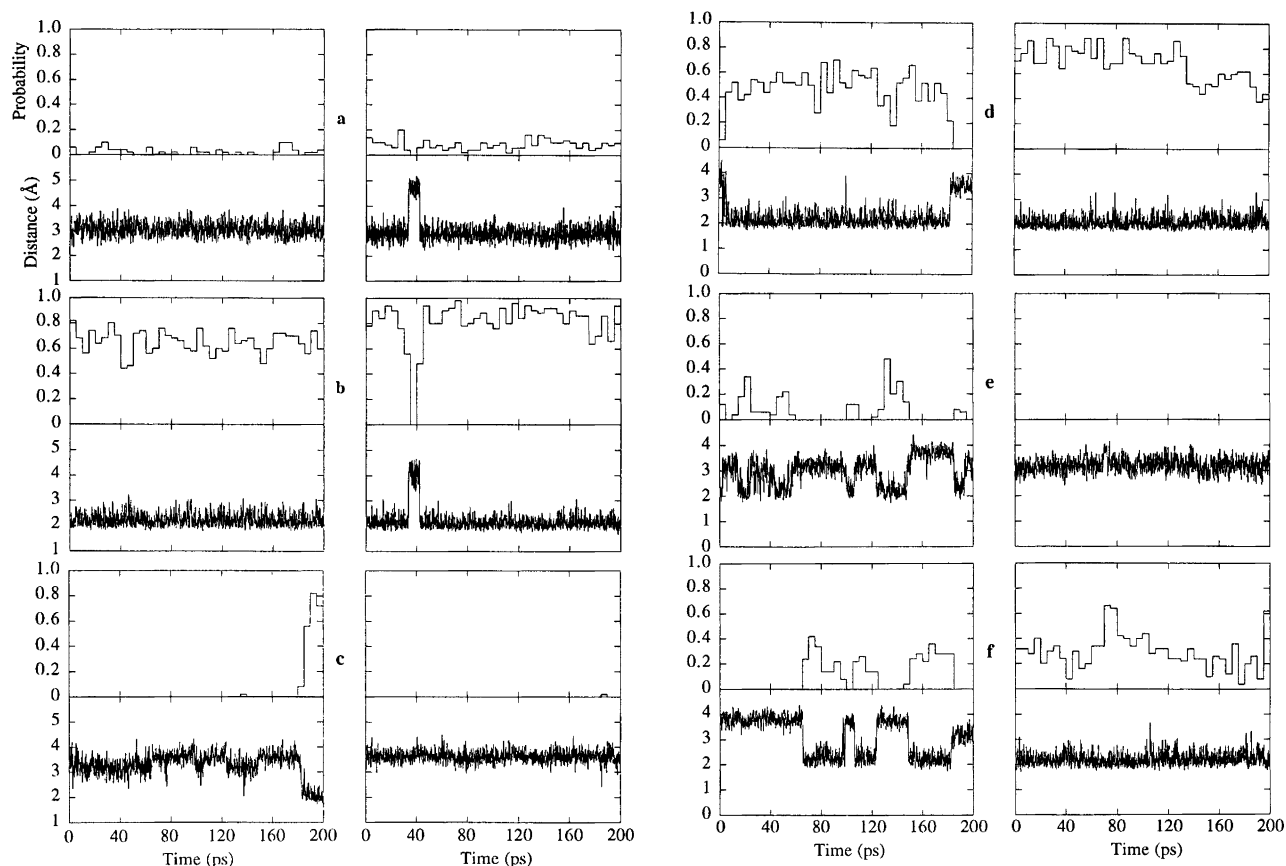


Fig. 3. Inter-atomic distances and H-bond probabilities (5 ps window) as a function of time in water (left column) and in DMSO (right column): (a) O1g...H' 6f, (b) O5g...H' 6f, (c) O2g...H' 1f, (d) H' 2g...O1f, (e) O1f...H' 3f, (f) H' 1f...O3f.

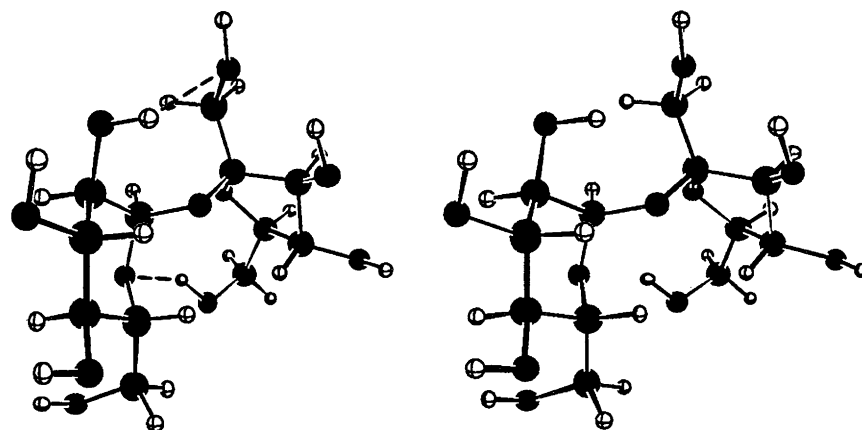


Fig. 4. Snapshot in stereo of sucrose in water. Inter-residue H-bonds $O5g \cdots H'6f$ and $H'2g \cdots O1f$ are indicated by dashed lines.

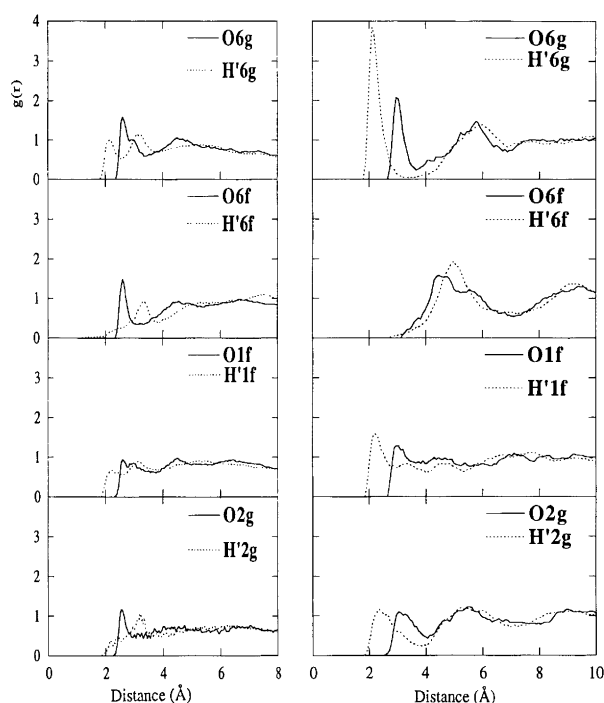


Fig. 5. Radial pair distribution functions, $g_{OO}(r)$ (solid line) and $g_{HO}(r)$ (dashed line) about the O6g, O6f, O1f and O2g hydroxyl groups in water (left column) and in DMSO (right column).

sented except for H'6f, but the second maximum is not as well pronounced.

The radial distribution functions for the ring and glycosidic linkage oxygens are different compared to those of the hydroxyl groups both in water and in DMSO (Fig. 6) and have lower coordination numbers (Table 4). In water the glycosidic linkage oxygen has a value of 0.5 and ring oxygen values around 1, compared to >3 for a number of the hydroxyl groups. The hydrogen bonding of water with these oxygen atoms as hydrogen acceptors is scarce, of the order of a few percent of the hydroxyl groups.

Table 4. Hydrogen bonds and coordination numbers for sucrose in water.^a

Solute atom	<H-bond>	$g(r)$
O1g	0.01	0.5
O2g	1.06	2.2
O3g	1.04	3.4
O4g	0.93	3.0
O5g	0.07	1.1
O6g	1.34	3.3
O1f	0.77	2.7
O3f	1.00	3.1
O4f	1.00	3.0
O5f	0.14	1.0
O6f	1.23	2.1
H'2g	0.26	0.24
H'3g	0.54	0.65
H'4g	0.53	0.65
H'6g	0.52	0.66
H'1f	0.43	0.43
H'3f	0.44	0.61
H'4f	0.62	0.79
H'6f	0.08	0.10

^a $\langle \cdots \rangle$ indicates an average value over the simulation.

Translational diffusion. Diffusion coefficients were calculated for the solute and solvent from the limiting slopes of the mean-square displacements.³⁷ The translational diffusion coefficients were also calculated from the velocity correlation functions³⁷ for the solvents. Sucrose had a value of 1.2×10^{-5} and $0.13 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ in water and in DMSO, respectively, as calculated from the limiting slopes of the mean-square displacements. The experimentally measured value for sucrose in water is $0.52 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ at 298 K.⁴⁰ In the aqueous simulation calculated values for water of 4.6×10^{-5} and $4.0 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ were obtained from the mean square displacement and velocity correlation function, respectively, for all the water molecules in the simulation cell. The values for the DMSO simulation were found to be 0.33×10^{-5} and $0.28 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ respectively. At 303 K pure water has an experimental diffusion coefficient of $2.6 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$.⁴¹ Both the sucrose and water

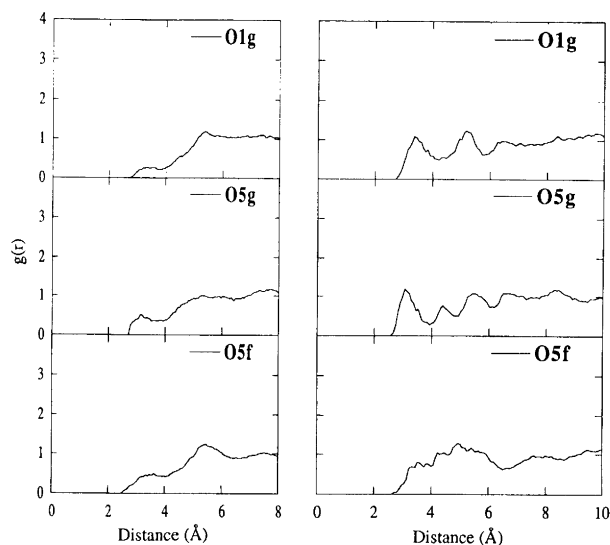


Fig. 6. Radial pair distribution functions, $g_{OO}(r)$, about the O1g, O5g and O5f ring oxygens in water (left column) and in DMSO (right column).

show a larger diffusion coefficient in the simulation than compared to experiment, but this is often seen for the models used at the present time.^{38,42} DMSO in a mixture of water and DMSO (68:32) should have a diffusion coefficient around $0.4 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ at 305 K,⁴³ and the simulated value around $0.3 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ for the DMSO molecules seems very reasonable. The lower value of $0.13 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ for sucrose in the simulation with DMSO as solvent is also reasonable.

Conclusions

In the present simulations of sucrose in water and in DMSO the conformation is similar to the crystal structure. Furthermore, the conformation of sucrose hardly differs between the two solvents. No transitions are observed to other ϕ/ψ regions that can be populated.⁸ This does not necessarily imply that sucrose is a very rigid molecule, as the length of the simulations was limited. NOE data⁷ are not explained by the proton-proton distances of non-exchangeable protons between residues simulated herein. The average values of the dihedral angle ϕ from the simulations are not in agreement with those derived from a Karplus-type relationship and NMR measurements of long-range ^1H , ^{13}C coupling constants between H1g and C2f,¹⁶ where the $^3J_{\text{C,H}}$ values were very similar for sucrose in D_2O and in DMSO. Inter-residue hydrogen bonding is to a large extent observed for H'6f to O5g and for H'2g to O1f, in both solvents. This inter-residue hydrogen bonding reduces transitions of these hydroxyl groups compared with those hydrogen bonding to solvent. The effect of intra-sucrose hydrogen bonding is also observed in the radial distribution functions, as maxima for first-shell coordination to solvent are reduced to a large extent or not present at all. Hydroxyl groups

interacting mainly with water show anticipated $g_{OO}(r)$ of ~ 3 . Future simulations of sucrose should be prolonged to the extent that energetically accessible conformers are sufficiently populated, either by molecular dynamics or Monte Carlo simulations, in order to facilitate comparison to experimental data from NMR experiments, especially NOE experiments.

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