

Supplementary Information

Structural Comparison between Sucrose and Trehalose in Aqueous Solution

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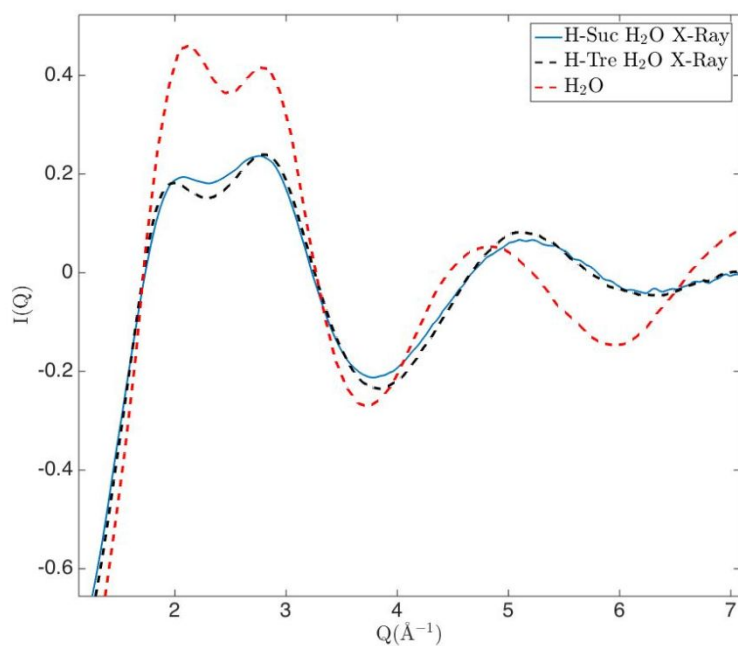


Figure S1. Zoomed in differential scattering cross sections for X-ray scattering on aqueous sucrose (blue line), trehalose (black dashed line) and bulk water (red dashed-dotted lines).

EPSR analysis

In this section we present further details, results, and discussion related to the EPSR analysis. As mentioned in the main article, the fits from the EPSR model (see figures S2 and S3 for sucrose and trehalose fits respectively) show larger discrepancies with the data than the two data sets show from each other, and therefore the given results may contain errors which are larger than the actual differences between the sugars as presented here. Nonetheless, EPSR is a widely used modeling technique which is capable of finding a molecular model of a system which is in agreement (within the experimental errors) with wide to intermediate angle scattering data. Since the original intra- and inter-molecular potential is based on typical force-fields parameters used in MD simulations, the agreement with the scattering data should be better than in an MD simulation based on the same force-fields. However, when comparing two solutions with such small overall structural differences as in the present case the accuracies of the structural models are too poor to make definite conclusions about structural differences from only the EPSR produced structural models, as mentioned in the main article.

Table S1. Lennard-Jones parameters used for the reference potential in the EPSR model. The atom type the different atom labels refer to can be seen in figure 1, apart from the carbon bonded hydrogen atoms, labelled M, which were omitted from that figure. The atom label O4 exclusively exists on the sucrose molecule. Furthermore, the Hw-Hw distances were constrained to a minimum distance of 1.58 Å to avoid unphysically close distances.

<i>Atom label</i>	<i>Epsilon (kJ/mol)</i>	<i>Sigma (Å)</i>	<i>Charge(e)</i>
<i>Hw</i>	0	0	0.4238
<i>Ow</i>	0.65	3.166	-0.8476
<i>O</i>	0.71128	3.1	-0.5
<i>O1</i>	0.58576	2.9	-0.5
<i>O2</i>	0.58576	2.9	-0.5
<i>O3</i>	0.71128	3.1	-0.5
<i>O4 (For sucrose)</i>	0.71128	3.1	-0.5
<i>H</i>	0.05	1.7	0.3005
<i>M</i>	0.12552	1.7	0.0
<i>C</i>	0.27614	3.5	0.258

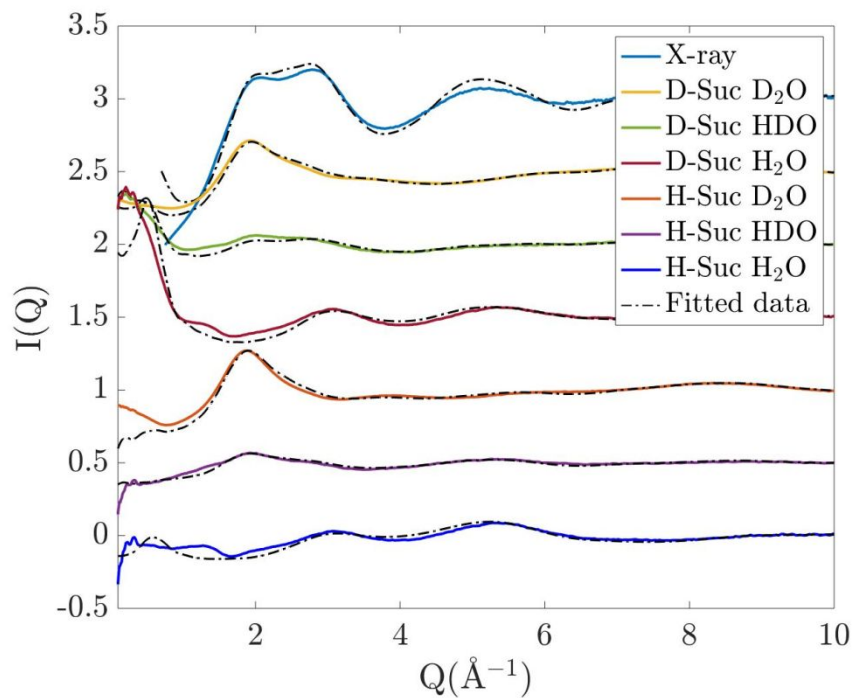


Figure S2. Differential scattering cross sections of all sucrose isotope compositions, with corresponding EPSR fits (dashed-dotted lines).

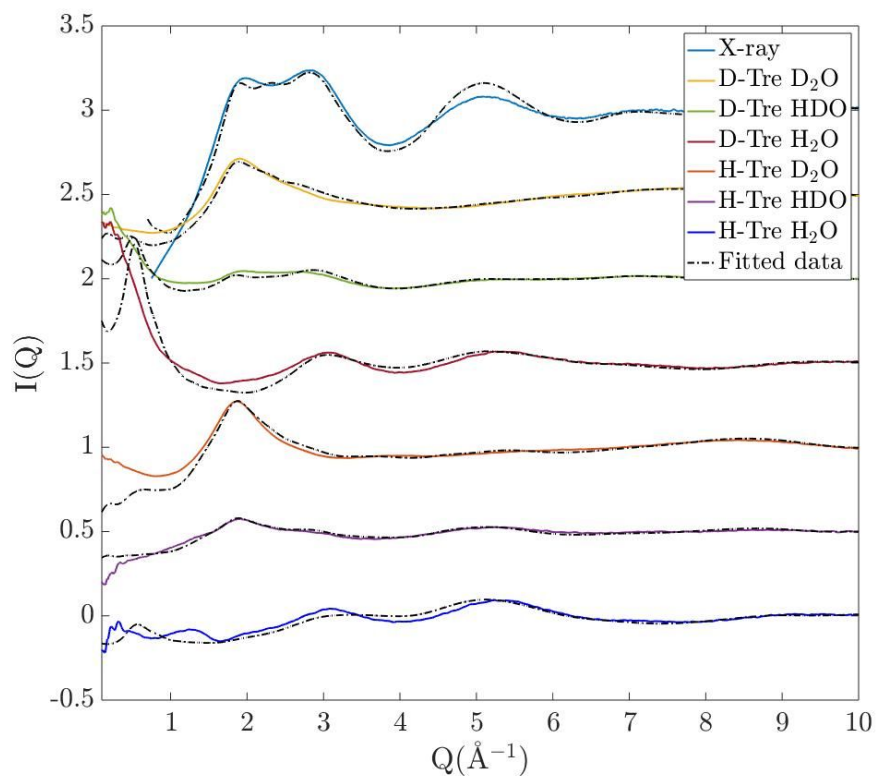


Figure S3. Differential scattering cross sections of all trehalose isotope compositions, with corresponding EPSR fits (dashed-dotted lines).

Water structure

The analysis of the $I(Q)$:s presented in the main text suggested a small difference in the solutions structure of water. This aspect was examined by analysis of the triplet Ow-Ow-Ow angle distribution obtained from the EPSR-models of the solutions and is presented in figure S4. Here it can be seen that both disaccharides promote a deviation of the water molecules from a bulk-like tetrahedral structure, however the deviation is significantly larger in the case of trehalose. This suggests that trehalose has a stronger perturbing effect on the water structure compared to sucrose, which is in line with what was seen in the analysis of $I(Q)$ in the main text. This aspect can also be seen in figure S5, which shows the partial pair correlation functions of the different water atoms.

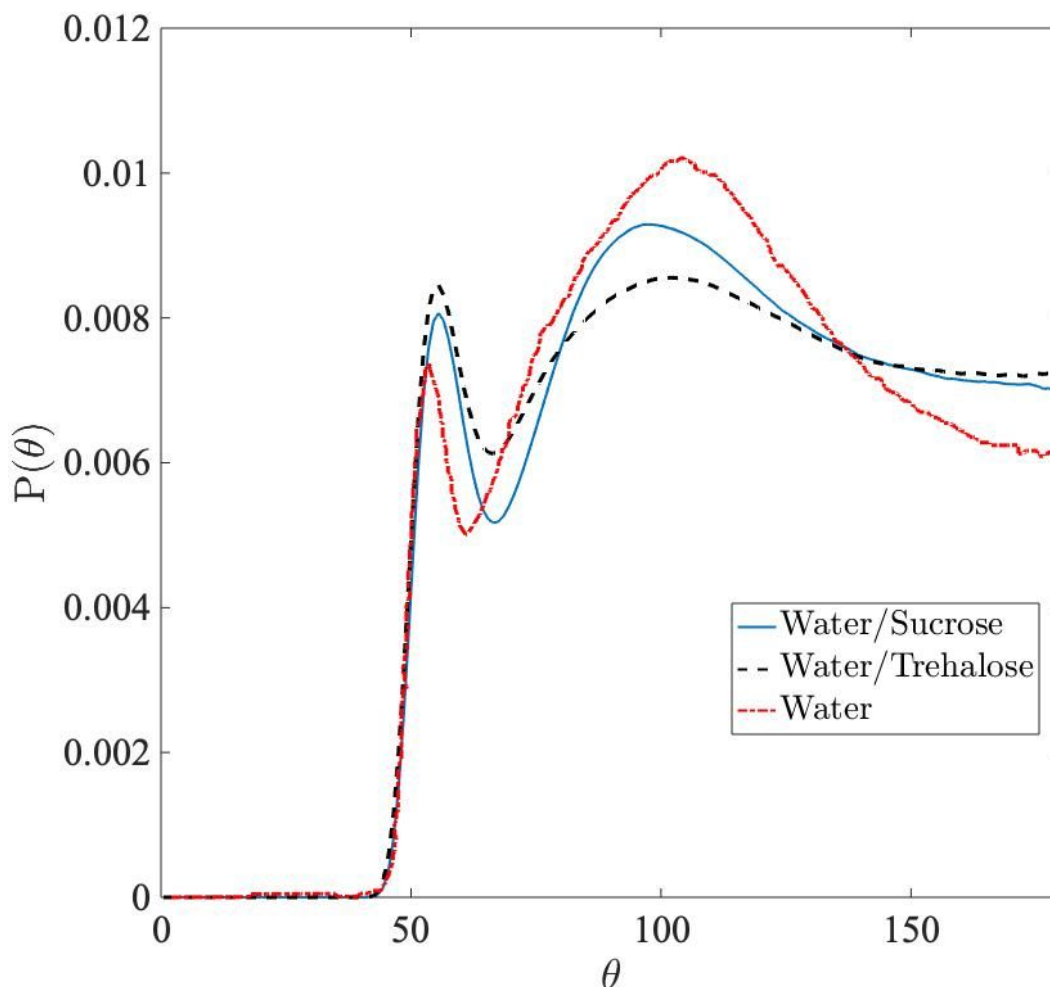


Figure S4. Angular distributions of triplets of water oxygens, where the middle oxygen is within 3.4 Å of the other two. Data are shown for water in sucrose solution (blue solid line), trehalose solution (black dashed line) and bulk water (red dotted line). Bulk water data were obtained from Dhabal et al.¹ The water/sugar data are based on EPSR simulation models.

In order to quantify the destructuring effect even further, we calculated the tetrahedrality parameter, based on the Ow-Ow-Ow distribution presented in figure S4. This parameter (often denoted as q) is calculated as²:

$$q = 1 - \frac{9 \int_0^\pi P(\theta) \left(\cos(\theta) + \frac{1}{3} \right)^2 \sin(\theta) d\theta}{4 \int_0^\pi P(\theta) \sin(\theta) d\theta} \quad (3)$$

where θ is the Ow-Ow-Ow angle, and $P(\theta)$ is the probability distribution of this angle (see figure S4). For a perfectly tetrahedral structure, q equals 1, and for a completely disordered system it is 0. For sucrose and trehalose the q parameters are 0.49 and 0.45 respectively. For the bulk water structure at 298K (based on an SPC model for water, as calculated by Dhabal et al¹), the order parameter q is 0.511. The q -parameter in the sucrose and trehalose systems is thus decreased by 5% and 12% respectively. It should however be noted that this value appears to be highly dependent on the molecular model (which can be seen in figure 2 of Ref. 1). For example, according to another study presented by Duboué-Dijon and Laage³, q is 0.67 for bulk water at 298 K.

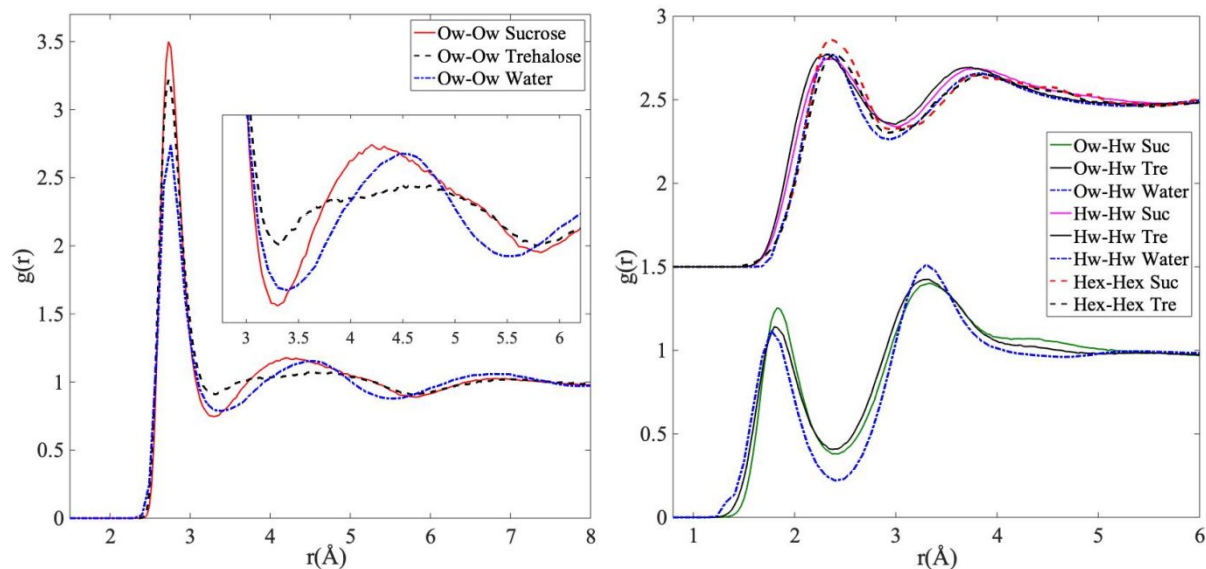


Figure S5. Partial pair correlation functions for different water atom pairs obtained from EPSR simulations. Solid coloured lines correspond to correlations in the water–sucrose solution, solid black lines represent the corresponding correlations in the water–trehalose solution, and dashed-dotted blue lines represent the same correlations for bulk water (obtained from Refs. 4,5). Left figure shows the Ow-Ow correlations, with the inset showing a zoomed in portion of the pair correlation function around 4.5 Å. Right figure shows Ow-Hw correlations in the lower curves, and Hw-Hw correlations in the upper curves. The Hw-Hw correlations are also plotted together with the experimentally obtained Hex-Hex correlations (red dashed for sucrose and black dashed for trehalose). These were obtained by taking the Fourier transform of $(I_{DDD}(Q) + I_{DHH}(Q)) - 2(I_{DHD}(Q))$, which removes all correlations except for the exchangeable hydrogen atoms (Hw and H), however the majority of the signal originates from the Hw-Hw atoms (since they are more abundant). The intramolecular peaks below ~ 2 Å have been omitted in this graph.

Disaccharide–water interactions

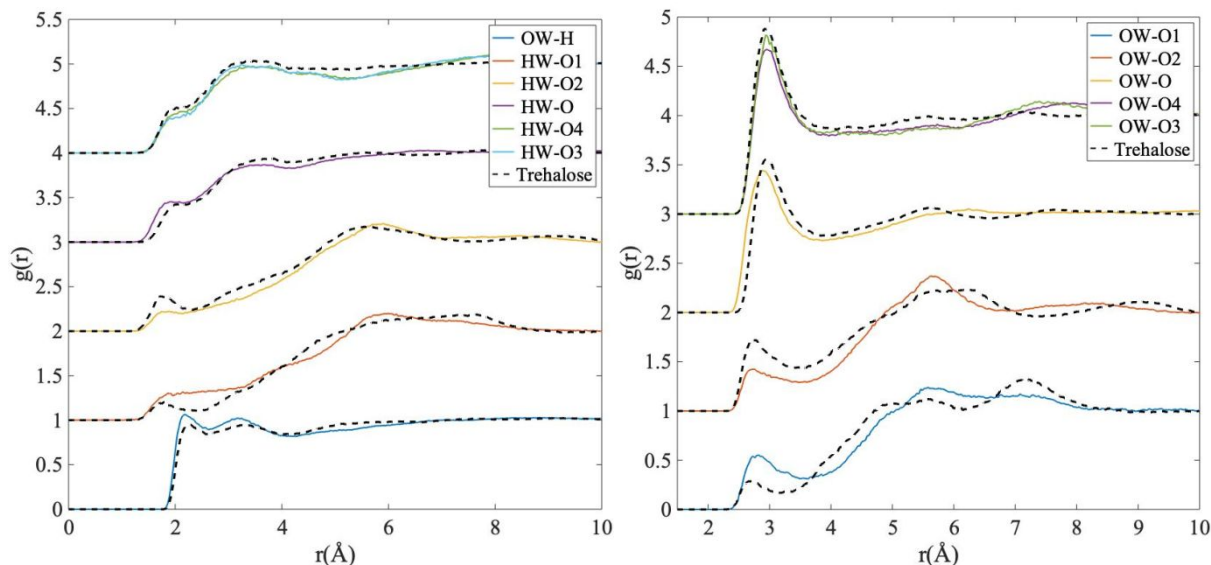


Figure S6. Partial pair correlation functions, $g_{ij}(r)$, for oxygen to hydrogen (left) and oxygen to oxygen (right), between sugar and water molecules. $g_{ij}(r)$'s of the sucrose solution are shown by colored lines, whereas analogous $g_{ij}(r)$'s for the trehalose solution are represented by black dashed lines. These partial pair correlation functions are obtained from EPSR simulations and therefore it should be noted that all the observed differences between the two sugar solutions cannot be experimentally established (see SI text below).

Figure S6 shows partial pair correlation functions, $g_{ij}(r)$, of water–trehalose and water–sucrose correlations. As mentioned above, details of the structural differences between the two solutions cannot be established from the simulations, but nevertheless it is interesting to note certain differences between the two disaccharides from these models. The most pronounced differences are seen for the O1 and O2 correlations (both with water hydrogens and oxygens), where sucrose exhibits a larger first peak for O1 correlations and trehalose exhibits a larger first peak for the O2 correlations. By summarizing the total amount of water molecules within 3.4 Å (as used in e.g. Refs. 1,6,7 as a cut-off distance for calculating the hydration number) of the different disaccharide sites listed in table 1, one finds that the two disaccharides are similarly hydrated, i.e. they are surrounded by a similar amount of water molecules (the exact numbers may differ slightly due to that the models are not in perfect agreement with the experimental data).

The number of hydrogen bonds was also calculated, using the three different hydrogen bonding criteria, for all the collected configurations of both disaccharides. Sucrose exhibits in general slightly more hydrogen bonding with waters than trehalose, however very similar numbers are obtained for the strongest coupled bonds (criteria 3).

Table S2. Coordination numbers (n_{α}^{β}) and number of hydrogen bonds (n_{HB}), as determined by different criteria for oxygen–oxygen or oxygen–hydrogen pairs between water and sucrose or trehalose (values given in parentheses are trehalose values). N_{tot} is the total number of water molecules coordinated or bonded to a single disaccharide. For sucrose, the sum consists of one O1-Ow/Hw, two O2-Ow/Hw, one O3-Ow/Hw, two O4-Ow/Hw, and 5 times each O-Ow/Hw number, plus eight H-Ow specifically for counting oxygen-hydrogen coordination numbers. For trehalose, the same summation applies with the only differences that there are two O3-Ow/Hw, six O-Ow/Hw, and no O4-Ow/Hw coordinations (since atom type O4 is not a label for trehalose).

α - β	r_{min}^1 (Å)	r_{peak}^2 (Å)	n_{α}^{β} ³	n_{HB} Criteria 1	n_{HB} Criteria 2	n_{HB} Criteria 3
O-Ow	4.0 (4.0)	2.9 (3.0)	2.82 (2.76)	N/A	1.12 (1.19)	0.16 (0.17)
O1-Ow	3.5 (3.2)	2.9 (2.7)	1.09 (0.55)	N/A	0.57 (0.36)	0.11 (0.10)
O2-Ow	3.5 (3.5)	2.8 (2.7)	0.86 (1.40)	N/A	0.42 (0.64)	0.15 (0.13)
O3-Ow	3.9 (3.9)	3.0 (3.0)	3.11 (3.34)	N/A	1.49(1.55)	0.19 (0.23)
O4-Ow	3.9	3.0	2.95	N/A	1.42	0.18
H-Ow	2.6 (2.6)	2.2 (2.3)	N/A	0.86 (0.74)	N/A	N/A
O-Hw	2.2 (2.2)	1.9 (2.0)	N/A	1.15 (0.97)	N/A	N/A
O1-Hw	N/A (2.4)	N/A (1.7)	N/A	0.79 (0.37)	N/A	N/A
O2-Hw	N/A(2.2)	1.8 (1.7)	N/A	0.55 (0.79)	N/A	N/A
O3-Hw	N/A	N/A	N/A	1.05 (1.24)	N/A	N/A
O4-Hw	N/A	N/A	N/A	1.10	N/A	N/A
N_{tot}	N/A	N/A	25.9 (26.6)	17.8 (16.1)	11.3 (11.8)	1.8 (1.8)

¹ First minima after first peak in $g(r)$

² Peak position of the first peak

³ Coordination number first shell. $d_{\text{oo}} < 3.4 \text{ \AA}$

References – Supplementary Information

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