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Hydration Structure of the Urea Molecule in Highly Concentrated Aqueous Solutions

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Neutron diffraction measurements with ^{14}N/^{15}N and H/D isotopic substitution methods have been carried out on aqueous 15 mol% urea solutions, in order to obtain information on the hydration structure of the amino group within the urea molecule in concentrated aqueous solutions. The observed first-order difference function, $^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q)$, and the N–H partial structure factor, $a_{\mathrm{NH}}(Q)$, were analyzed by the least squares fitting procedure. The nearest neighbor N···O and N···H distances were obtained to be 2.92(1) Å and 3.42(1) Å, respectively. The average hydration number per one amino group was determined to be 2.0(1). The tilt angle between the N–H···O axis and the molecular plane of the hydrogen bonded water molecule is estimated to be 51(5)°.

The hydration structure of the urea molecule has received much attention because of its importance for the understanding of reaction mechanisms occurring in various biochemical systems. Earlier X-ray diffraction work by Adams et al. evidenced the "structure-breaking" effect of urea molecules on tetrahedrally hydrogen-bonded bulk water.[1] On the other hand, recent molecular dynamics (MD) simulations on aqueous urea solutions have shown that the urea molecule has little effect on bulk water structure beyond the first hydration shell.[2–4] The experimental H–H partial distribution function, $g_{\mathrm{HH}}(r)$, derived from the neutron diffraction with H/D isotopic substitution method has confirmed that intermolecular hydrogen bonds among water molecules are still maintained in highly concentrated aqueous 10 m (15.3 mol%) urea solutions.[5] In order to clarify the effect of the urea molecule on the hydrogen-bonded network of the bulk water, it is necessary to obtain detailed information concerning the hydration structure of the urea molecule itself at the partial structure function level.

Turner et al. carried out the first attempt to resolve the partial structure function around the amino group of the urea molecule in aqueous solution by employing neutron diffraction with ^{14}N/^{15}N isotopic substitution technique.[6–9] The partial distribution function, $\mathrm{G_N}(r)$, around the amino nitrogen atom was successfully obtained; however, the hydration geometry of the nearest neighbor D_2O molecule around the amino group could not be determined because of considerable overlap of intra- and intermolecular contributions in the observed $\mathrm{G_N}(r)$. The number of D_2O molecules in the first hydration shell of the urea molecule in the 2 m (3.8 mol%) heavy water solution was roughly estimated to be 7.1(5) through an integration of the observed $\mathrm{G_N}(r)$ from $r = 2.55$ to 4.00 Å.[6–8] The concentration dependence of the $\mathrm{G_N}(r)$ function for aqueous urea solutions has been examined by Turner et al.[9] The $\mathrm{G_N}(r)$ function observed for 2, 7 and 14 m urea solutions indicated that there is remarkably little change in the intermolecular structure around the urea molecule.[9] In order to determine the hydration geometry of water molecules in the first hydration shell of the urea molecule, it is necessary to distinguish partial distribution functions, $g_{\mathrm{NO}}(r)$ and $g_{\mathrm{NH}}(r)$, from observed $\mathrm{G_N}(r)$ functions in which all the contributions from the N-α (α: N, O, H, and C) pairs are involved. A combination of the ^{14}N/^{15}N and H/D isotopic substitution methods is therefore indispensable. Turner et al. have reported $\Delta_{\mathrm{N}}(Q)$ and corresponding $\mathrm{G_N}(r)$ functions observed for 2.0 and 7.0 m urea solutions in H_2O–D_2O mixtures.[10,11] However, no definite conclusions concerning the nearest neighbor N–O and N–H correlations have been drawn. In order for one to deduce the N–H partial structure factor, at least four independent measurements are necessary on sample solutions in which both ^{14}N/^{15}N and H/D isotopic ratios have been changed. Samples with larger differences in the scattering lengths of the hydrogen atoms are preferred. Turner et al. employed relatively lower H_2O contents (30% H_2O for 7.0 m and 40% H_2O for 2.0 m solutions, respectively), which would make the separation of the N–O and N–H contributions difficult. Moreover, overlapping between the intra- and intermolecular contributions has caused an additional difficulty in investigating the hydration geometry of the nearest neighbor water molecules around the amino group.

In this paper, we describe results of neutron diffraction measurements on concentrated aqueous 15 mol% urea solutions with different ^{14}N/^{15}N and H/D isotopic compositions. The difference function, $^{\mathrm{D}}\Delta_{\mathrm{N}}(Q)$, from two ^{14}N/^{15}N isotopically substituted solutions, $[(^{14}\mathrm{ND_2})_2\mathrm{C{=}O}]_{0.15}(\mathrm{D_2O})_{0.85}$ and $[(^{15}\mathrm{ND_2})_2\mathrm{C{=}O}]_{0.15}(\mathrm{D_2O})_{0.85}$, in conjunction with that, $^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q)$, from two solutions, $[(^{14}\mathrm{N}^{0}\mathrm{H_2})_2\mathrm{C{=}O}]_{0.15}(^{0}\mathrm{H_2O})_{0.85}$ and $[(^{15}\mathrm{N}^{0}\mathrm{H_2})_2\mathrm{C{=}O}]_{0.15}(^{0}\mathrm{H_2O})_{0.85}$, gives information concerning partial structure factors, $a_{\mathrm{NH}}(Q)$, and to a good approximation, $a_{\mathrm{NO}}(Q)$, for the first hydration shell of the amino group within the urea molecule. In the latter two solutions, the mean scattering length of hydrogen atoms was set to be zero, which enables us to simplify the interpretation of the observed ${}^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q)$ function. Moreover, the intramolecular contribution within the urea molecule was subtracted from the observed $\Delta_{\mathrm{N}}(Q)$ function in order to avoid overlap of the intra- and intermolecular contributions in the observed distribution function around the nitrogen atom.

Experimental

Materials. Isotopically enriched $({}^{15}\mathrm{NH_2})_2\mathrm{C{=}O}$ (98.0% ^{15}N, Isotec Inc.) and natural $({}^{14}\mathrm{NH_2})_2\mathrm{C{=}O}$ (99.6% ^{14}N, Nacalai Tesque, guaranteed grade) were deuterated by dissolving them repeatedly into D_2O (99.9%, Aldrich Chemical Co. Inc.), followed by the dehydration under vacuum. The required amounts of enriched compounds, $({}^{15}\mathrm{ND_2})_2\mathrm{C{=}O}$ and $({}^{14}\mathrm{ND_2})_2\mathrm{C{=}O}$, were dissolved into D_2O or D_2O/H_2O mixtures to prepare four kinds of aqueous 15 mol% urea solutions with different isotopic compositions, I: $[({}^{14}\mathrm{ND_2})_2\mathrm{C{=}O}]_{0.15}(\mathrm{D_2O})_{0.85}$, II: $[({}^{15}\mathrm{ND_2})_2\mathrm{C{=}O}]_{0.15}(\mathrm{D_2O})_{0.85}$, III: $[({}^{14}\mathrm{N}{}^{0}\mathrm{H_2})_2\mathrm{C{=}O}]_{0.15}({}^{0}\mathrm{H_2O})_{0.85}$, and IV: $[({}^{15}\mathrm{N}{}^{0}\mathrm{H_2})_2\mathrm{C{=}O}]_{0.15}({}^{0}\mathrm{H_2O})_{0.85}$. The superscript "0" denotes an isotopic mixture in which the mean scattering length of hydrogen atoms is zero ($b_{\mathrm{H}} = 0$). Each sample solution that was sealed into a cylindrical quartz cell (11.6 mm in inner diameter and 1.2 mm in thickness) and used for the neutron diffraction measurement. Sample parameters are summarized in Table 1.

Neutron Diffraction Measurements. Neutron diffraction measurements were carried out at 25 °C using an ISSP 4G (GPTAS) diffractometer installed at the JRR-3M research reactor operated at 20 MW in the Japan Atomic Energy Research Institute (JAERI), Tokai, Japan. The incident neutron wavelength, $\lambda = 1.100 \pm 0.003$ Å, was determined by Bragg reflections from KCl powder. Collimations used were 40′–80′–80′ in going from the reactor to the detector. The aperture of the collimated beam was 15 mm in width and 30 mm in height. Scattered neutrons were collected over the angular range of $3.0 \le 2\theta \le 115°$, which corresponds to $0.30 \le Q \le 9.63$ Å^{-1} (the scattering vector magnitude, $Q = 4\pi \sin\theta/\lambda$). The step interval was chosen to be $\Delta(2\theta) = 0.5°$ in the range of $3 \le 2\theta \le 40°$ and $\Delta(2\theta) = 1°$ in the range of $41 \le 2\theta \le 115°$, respectively. The preset neutron monitor counts were 1.2×10^9 for sample solutions. The total number of observed counts was at least 1.2×10^5 counts, and ranged over as high as 4.0×10^5 counts. Scattering intensities were measured in advance for a vanadium rod (5.8 mm in diameter), empty cell and background, respectively.

Data Reduction. Observed scattering intensities from the sample were corrected for instrumental background, absorption,[12] and multiple scattering.[13] The obtained count rate for the sample was converted to the absolute scale by the use of scattering intensities from the vanadium rod. Details of the data correction and normalization procedure have already been described in our previous papers.[14,15]

The first-order difference function,[16,17] $\Delta_{\mathrm{N}}(Q)$, is defined as the numerical difference of normalized scattering cross sections from sample solutions, that are identical in isotopic composition of hydrogen atoms and differ in composition of the amino-nitrogen atoms within the urea molecule:

$$
\begin{aligned}
{}^{\mathrm{D}}\Delta_{\mathrm{N}}(Q) = {} & (\mathrm{d}\sigma/\mathrm{d}\Omega)^{\mathrm{obs}} \text{ (for sample I)} \\
& - (\mathrm{d}\sigma/\mathrm{d}\Omega)^{\mathrm{obs}} \text{ (for sample II)},
\end{aligned} \tag{1}
$$

$$
\begin{aligned}
{}^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q) = {} & (\mathrm{d}\sigma/\mathrm{d}\Omega)^{\mathrm{obs}} \text{ (for sample III)} \\
& - (\mathrm{d}\sigma/\mathrm{d}\Omega)^{\mathrm{obs}} \text{ (for sample IV)}.
\end{aligned} \tag{2}
$$

The $\Delta_{\mathrm{N}}(Q)$, scaled at the stoichiometric unit, $[({}^{*}\mathrm{N}{}^{*}\mathrm{H_2})_2\text{-}\mathrm{C{=}O}]_x({}^{*}\mathrm{H_2O})_{1-x}$, can be expressed as the weighted sum of four partial structure factors;

$$
\begin{aligned}
\Delta_{\mathrm{N}}(Q) = {} & A[a_{\mathrm{NO}}(Q) - 1] + B[a_{\mathrm{NH}}(Q) - 1] \\
& + C[a_{\mathrm{NC}}(Q) - 1] + D[a_{\mathrm{NN}}(Q) - 1],
\end{aligned} \tag{3}
$$

where, $A = 4x(b_{\mathrm{N}} - b'_{\mathrm{N}})b_{\mathrm{O}}$, $B = 8x(1 + x)(b_{\mathrm{N}} - b'_{\mathrm{N}})b_{\mathrm{H}}$, $C = 4x^2(b_{\mathrm{N}} - b'_{\mathrm{N}})b_{\mathrm{C}}$, and $D = 4x^2(b_{\mathrm{N}}{}^2 - b'_{\mathrm{N}}{}^2)$, respectively. The weighting factors *A*–*D* in Eq. 3 are numerically listed in Table 2. The intramolecular contribution, $I^{\mathrm{intra}}(Q)$, from the $\mathrm{N}\cdots\alpha$ pair within the urea molecule is calculated by

$$
\begin{aligned}
I^{\mathrm{intra}}(Q) = {} & \Sigma\, 2c_{\mathrm{N}}b_{\alpha}(b_{\mathrm{N}} - b'_{\mathrm{N}})\exp(-l_{\mathrm{N}\alpha}{}^2Q^2/2)\sin(Qr_{\mathrm{N}\alpha})/ \\
& (Qr_{\mathrm{N}\alpha}),
\end{aligned} \tag{4}
$$

where, c_{N} denotes the number of N atoms in the stoichiometric unit. Parameters, $l_{\mathrm{N}\alpha}$ and $r_{\mathrm{N}\alpha}$ stand for the root mean square displacement and internuclear distance for the $\mathrm{N}\cdots\alpha$ pair, respectively. Values of $r_{\mathrm{N}\alpha}$ and $l_{\mathrm{N}\alpha}$ used for the present analysis were taken from the literature determined from the single-crystal neutron diffraction work[18] and from values calculated for related molecules,[19,20] respectively. The calculated $I^{\mathrm{intra}}(Q)$ was then subtracted from the observed $\Delta_{\mathrm{N}}(Q)$ to obtain the intermolecular difference function, $\Delta_{\mathrm{N}}{}^{\mathrm{inter}}(Q)$,

$$
\Delta_{\mathrm{N}}{}^{\mathrm{inter}}(Q) = \Delta_{\mathrm{N}}(Q) - I^{\mathrm{intra}}(Q). \tag{5}
$$

The distribution function, $G_{\mathrm{N}}(r)$, around the nitrogen atom is obtained by the Fourier transform of the observed $\Delta_{\mathrm{N}}(Q)$,

$$
\begin{aligned}
G_{\mathrm{N}}(r) & = 1 + (A + B + C + D)^{-1}(2\pi^2\rho r)^{-1} \\
& \quad \times \int_0^{Q_{\max}} Q\Delta_{\mathrm{N}}(Q)\sin(Qr)\,\mathrm{d}Q \\
& = [Ag_{\mathrm{NO}}(r) + Bg_{\mathrm{NH}}(r) + Cg_{\mathrm{NC}}(r) + Dg_{\mathrm{NN}}(r)] \\
& \quad \times (A + B + C + D)^{-1}.
\end{aligned} \tag{6}
$$

The upper limit of the integral, $Q_{\max}$, was set to 9.63 Å^{-1}. The intermolecular distribution function, $G_{\mathrm{N}}{}^{\mathrm{inter}}(r)$ was evaluated by the Fourier transform of the $\Delta_{\mathrm{N}}{}^{\mathrm{inter}}(Q)$.

Table 1. Isotopic Compositions and Mean Scattering Lengths, b_{N} and b_{H}, of Nitrogen and Hydrogen Atoms, Total Cross Sections and the Number Density Scaled in the Stoichiometric Unit, $[({}^{*}\mathrm{N}{}^{*}\mathrm{H_2})_2\mathrm{C{=}O}]_{0.15}({}^{*}\mathrm{H_2O})_{0.85}$, σ_{t} and ρ, Respectively

Sample	^{14}N/%	^{15}N/%	H/%	D/%	$b_{\mathrm{N}}/10^{-12}$ cm	$b_{\mathrm{H}}/10^{-12}$ cm	σ_{t}/barns[a)]	ρ/Å^{-3}
I$[({}^{14}\mathrm{ND_2})_2\mathrm{C{=}O}]_{0.15}(\mathrm{D_2O})_{0.85}$	99.6	0.4	0.2	99.8	0.936	0.665	18.68	0.02115
II$[({}^{15}\mathrm{ND_2})_2\mathrm{C{=}O}]_{0.15}(\mathrm{D_2O})_{0.85}$	2.0	98.0	0.2	99.8	0.650	0.665	14.95	
III$[({}^{14}\mathrm{N}{}^{0}\mathrm{H_2})_2\mathrm{C{=}O}]_{0.15}({}^{0}\mathrm{H_2O})_{0.85}$	99.6	0.4	62.6	37.4	0.936	0.017	63.89	
IV$[({}^{15}\mathrm{N}{}^{0}\mathrm{H_2})_2\mathrm{C{=}O}]_{0.15}({}^{0}\mathrm{H_2O})_{0.85}$	2.0	98.0	62.5	37.5	0.650	0.021	61.59	

a) For incident neutron wavelength of 1.100 Å.

Table 2. Values of the Coefficients of $a_{ij}(Q)$ in Eq. 3.

Difference Function	A/barns	B/barns	C/barns	D/barns
$^{D}\Delta_{N}(Q)$	0.101	0.267	0.018	0.041
$^{0H}\Delta_{N}(Q)$	0.099	0.004	0.017	0.041

The second-order difference between $^{D}\Delta_{N}(Q)$ and $^{0H}\Delta_{N}(Q)$, in which the isotopic composition of hydrogen atoms was changed, can be well approximated as the intermolecular N–H partial structure factor, $a_{NH}(Q)$:

$$^{D}\Delta_{N}(Q) - {}^{0H}\Delta_{N}(Q) = 8x(1 + x)(b_{N} - b'_{N}) \times (b_{D} - b'_{^{0}H})[a_{NH}(Q) - 1]. \qquad (7)$$

The Fourier transform of the $a_{NH}(Q)$ gives the partial distribution function, $g_{NH}(r)$, corresponding to the distribution of hydrogen atoms belonging to the solvent water molecule:

$$g_{NH}(r) = 1 + (2\pi^{2}\rho r)^{-1}\int_{0}^{Q_{\max}} Q[a_{NH}(Q) - 1]\sin(Qr)\mathrm{d}Q. \qquad (8)$$

Results and Discussion

Scattering cross sections, $(\mathrm{d}\sigma/\mathrm{d}\Omega)^{obs}$, observed for isotopically different aqueous 15 mol% urea solutions are shown in Fig. 1. Although the overall features of $(\mathrm{d}\sigma/\mathrm{d}\Omega)^{obs}$ with different $^{14}N/^{15}N$ ratios look very similar, a systematic difference in the intensity can be observed around the first diffraction peak at $Q \approx 2$ Å^{-1}, corresponding to the difference in the scattering length of the amino-nitrogen atom. The decrease in the intensity of $(\mathrm{d}\sigma/\mathrm{d}\Omega)^{obs}$ at a larger-Q range due to the inelasticity effect becomes more pronounced for $^{0}H_2O$ solutions which have higher H content.

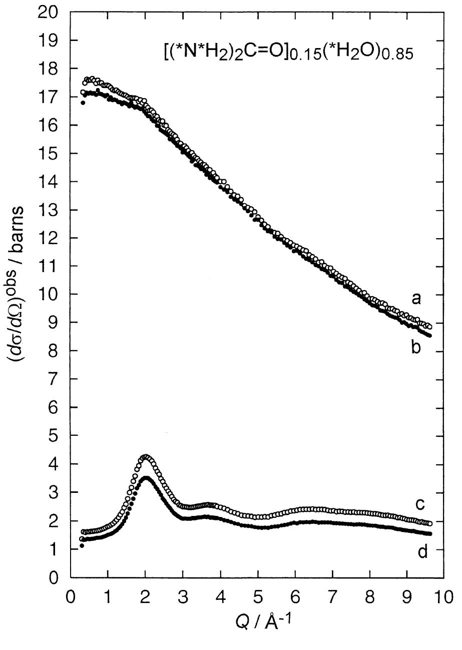

Fig. 1. Observed scattering cross sections $(\mathrm{d}\sigma/\mathrm{d}\Omega)^{obs}$ for aqueous 15 mol% urea solutions with different isotopic ratios of $^{14}N/^{15}N$ and H/D. a) ^{14}N–^{0}H. b) ^{15}N–^{0}H. c) ^{14}N–D. d) ^{15}N–D. The superscript 0 denotes the isotopic mixture in which the mean scattering length is zero.

In order to elucidate the environmental structure around the nitrogen atom within the urea molecule, the first-order difference functions, $^{D}\Delta_{N}(Q)$ and $^{0H}\Delta_{N}(Q)$, were evaluated by the numerical difference in the observed scattering cross sections between D_2O solutions, I – II and between $^{0}H_2O$ solutions III– IV, respectively. The observed difference function, $^{D}\Delta_{N}(Q)$, and the corresponding distribution function around the amino-nitrogen atoms within the urea molecule, $^{D}G_{N}(r)$, are represented in Figs. 2 and 3, respectively. In Fig. 2a, an evident first peak at $Q \approx 2$ Å^{-1} and oscillational feature of $^{D}\Delta_{N}(Q)$ extending to

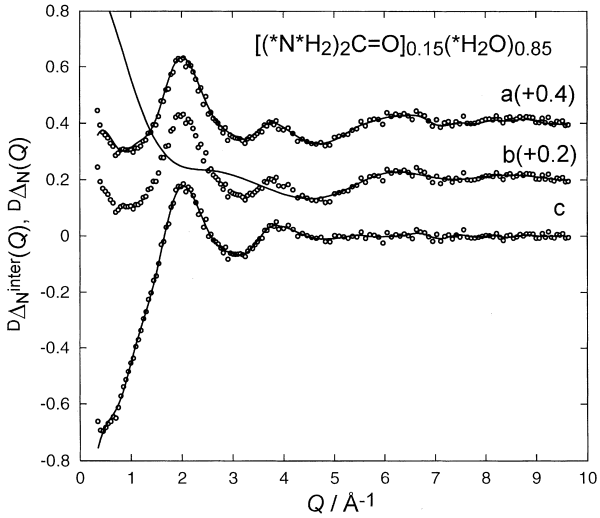

Fig. 2. a) Circles: The observed difference function, $^{D}\Delta_{N}(Q)$, for 15 mol% urea solution in D_2O. The solid line: The back Fourier transform of $^{D}G_{N}(r)$ shown by the solid line in Fig. 3a. b) Circles: The observed $^{D}\Delta_{N}(Q)$. The solid line: The intramolecular contribution within the urea molecule, $I^{intra}(Q)$. c) Circles: Th intermolecular difference function, $^{D}\Delta_{N}{}^{inter}(Q)$. The solid line: The back transform of $^{D}G_{N}{}^{inter}(r)$ indicated by the solid line in Fig. 3b.

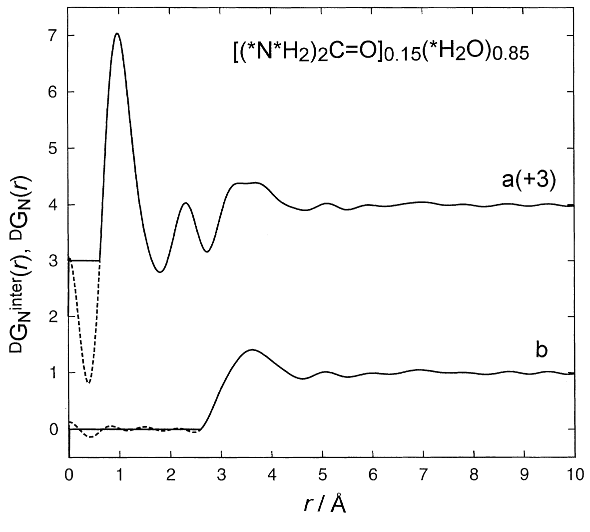

Fig. 3. a) The total and b) intermolecular distribution function around the amino-nitrogen atom of the urea molecule, $^{D}G_{N}(r)$ and $^{D}G_{N}{}^{inter}(r)$, respectively, observed for the 15 mol% urea solution in D_2O.

the higher-Q region, are clearly observed. The calculated intramolecular interference term, $I^{\mathrm{intra}}(Q)$ (Fig. 2b), was then subtracted from the observed ${}^{\mathrm{D}}\Delta_{\mathrm{N}}(Q)$. The normalization factor, β, defined by ${}^{\mathrm{D}}\Delta_{\mathrm{N}}(Q) = \beta \times I^{\mathrm{intra}}(Q)$ (in the sufficiently high-Q region), was obtained to be $\beta = 1.05 \pm 0.02$ from the least squares fit in the range of $5.0 \leq Q \leq 9.6$ Å^{-1}. The result implies that the present data correction and normalization procedures have been correctly carried out; the overall normalization error in the present ${}^{\mathrm{D}}\Delta_{\mathrm{N}}(Q)$ is roughly estimated to be within 5%. The intermolecular difference function, ${}^{\mathrm{D}}\Delta_{\mathrm{N}}{}^{\mathrm{inter}}(Q)$ (Fig. 2c), can be characterized by the first and the second diffraction peaks located at $Q \approx 2$ and 4 Å^{-1}, respectively.

Total and intermolecular distribution functions, ${}^{\mathrm{D}}\mathrm{G}_{\mathrm{N}}(r)$ and ${}^{\mathrm{D}}\mathrm{G}_{\mathrm{N}}{}^{\mathrm{inter}}(r)$, are shown in Figs. 3a and 3b. The first peak at $r \approx 1$ Å in the present ${}^{\mathrm{D}}\mathrm{G}_{\mathrm{N}}(r)$ (Fig. 3a) is assigned to the intramolecular N–D interactions within the urea molecule. Contributions from intramolecular N–C interactions may be contained in the higher-r side shoulder of this peak. The second peak at $r \approx 2.3$ Å can be ascribed to the sum of contributions from intramolecular non-bonding N···O, N···N and N···D interactions. The intermolecular ${}^{\mathrm{D}}\mathrm{G}_{\mathrm{N}}{}^{\mathrm{inter}}(r)$ shown in Fig. 3b has a broad first peak centered at 3.6 Å, in which interactions between amino-nitrogen atom and the nearest neighbor water molecules should be involved. However, details of hydration geometry cannot be obtained from the present ${}^{\mathrm{D}}\mathrm{G}_{\mathrm{N}}{}^{\mathrm{inter}}(r)$ function alone. The separation of the N–H and N–O partial structure factors is necessary.

Figure 4 represents the total and intermolecular first-order difference functions, ${}^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q)$ and ${}^{0\mathrm{H}}\Delta_{\mathrm{N}}{}^{\mathrm{inter}}(Q)$, respectively, between ${}^{0}\mathrm{H}_2\mathrm{O}$ solutions III and IV. A significant difference in the interference pattern between the ${}^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q)$ and ${}^{\mathrm{D}}\Delta_{\mathrm{N}}(Q)$ is noted. This difference can be regarded as the N–H partial structure factor. Data points of the present ${}^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q)$ seem more scattered in comparison with the ${}^{\mathrm{D}}\Delta_{\mathrm{N}}(Q)$, due to large incoherent scattering intensity from the H nuclei. In order to check uncertainties in the oscillational amplitude of the present ${}^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q)$ arising from errors in data correction and normalization procedures, the least squares fitting analysis was applied to the observed ${}^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q)$ in the range of $5.0 \leq Q \leq 9.6$ Å^{-1} with intramolecular interference term calculated as shown in Fig. 4b. The normalization factor obtained was 0.93 ± 0.05, suggesting that the normalization error involved in the present ${}^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q)$ can be estimated to ca. 7%. In the present ${}^{0\mathrm{H}}\Delta_{\mathrm{N}}{}^{\mathrm{inter}}(Q)$, the first diffraction peak at $Q \approx 2.5$ Å^{-1} is well identified.

The total and intermolecular distribution functions, ${}^{0\mathrm{H}}\mathrm{G}_{\mathrm{N}}(r)$ and ${}^{0\mathrm{H}}\mathrm{G}_{\mathrm{N}}{}^{\mathrm{inter}}(r)$, are represented in Figs. 5a and 5b, respectively; here the contributions from the N–H interaction are negligibly small, as indicated in Table 2. A well resolved first peak at $r = 1.3$ Å in the present ${}^{0\mathrm{H}}\mathrm{G}_{\mathrm{N}}(r)$ is reasonably ascribed to the intramolecular N–C interaction within the urea molecule. Contributions from intramolecular N···O and N···N interactions are involved in the second peak at $r = 2.2$ Å. Peaks appearing at $r = 3.0$ and 3.8 Å are attributable to the intermolecular interactions between the amino-nitrogen atom and oxygen atoms of neighboring water molecules. These peaks are observed as partially defined first and the second peaks in the intermolecular distribution function, ${}^{0\mathrm{H}}\mathrm{G}_{\mathrm{N}}{}^{\mathrm{inter}}(r)$ (Fig. 5b), implying that the amino group of the urea molecule has a stable hydration shell, which is consistent with the result derived from a recent MD study.[4] The nearest neighbor N···N interaction might be involved in the 3.8 Å peak if urea dimers exist in these solutions as has been predicted by an MD work by Åstrand et al.[2] On the other hand, Raman spectroscopic results by Hoccart and Turrel do not indicate the presence of a significant concentration of the urea dimers.[21] In order to examine the presence of the urea dimer in this solution, it is necessary to obtain the N–N partial distribution function, $g_{\mathrm{NN}}(r)$, which requires an additional measurement on the solution with nitrogen scattering length to be $(b_{^{14}\mathrm{N}} + b_{^{15}\mathrm{N}})/2$. This will be a future research subject.

In order to obtain more detailed information concerning hydration structure around the amino group of the urea, the least squares fitting procedure was applied to the observed ${}^{0\mathrm{H}}\Delta_{\mathrm{N}}(Q)$ and $a_{\mathrm{NH}}(Q)$ derived through Eq. 7. The model function, $I^{\mathrm{model}}(Q)$, consists of the short- and long-range interactions written as below.[22–24] The "short range" interaction means that

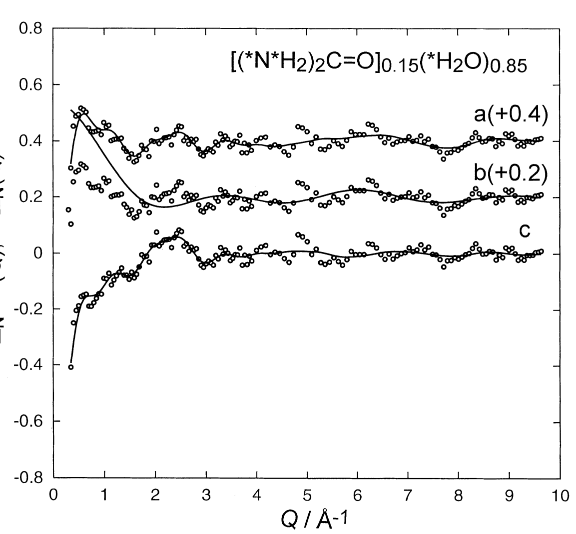

Fig. 4. Same notations as in Fig. 2 except for the 15 mol% urea solution in ${}^{0}\mathrm{H}_2\mathrm{O}$.

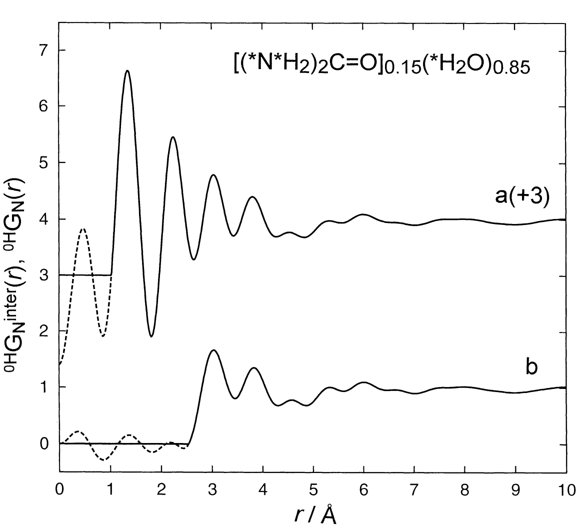

Fig. 5. Same notations as in Fig. 3 except for the 15 mol% urea solution in ${}^{0}\mathrm{H}_2\mathrm{O}$.

the *i–j* atomic distribution in the $r \cdot g_{ij}(r)$ can be approximated by a Gaussian distribution. The "long-range" interaction describes random distribution of atoms at the radial distance beyond r_0.

$$I^{\text{model}}(Q) = \Sigma\, 2c_N n_{N\alpha} b_\alpha (b_N - b'_N)\exp(-l_{N\alpha}^2 Q^2/2)\sin(Qr_{N\alpha})/(Qr_{N\alpha}) + 4\pi\rho W\exp(-l_0^2 Q^2/2)[Qr_0\cos(Qr_0) - \sin(Qr_0)]Q^{-3}, \qquad (9)$$

where, W is the coefficient describing the amplitude of the long-range interaction. For analysis of the $^{0\text{H}}\Delta_N^{\text{inter}}(Q)$, nearest neighbor N···O interactions are taken into account, i.e., $\alpha = \text{O}$ and $W = (A + B + C + D)$ are applied, while $\alpha = \text{H}$ and $W = 8x(1 + x)(b_N - b'_N)(b_D - b'_{0\text{H}})$ are employed for the analysis of the $a_{\text{NH}}(Q)$. Parameters, $n_{N\alpha}$ *and* b_α, corresponds to the coordination number of α (α = O, H) atom around the N atom and the coherent scattering length of the α atom, respectively. Values, $l_{N\alpha}$ and $r_{N\alpha}$, are the r.m.s. amplitude and internuclear distance for N···α pair, respectively. The long-range parameter, r_0, means the distance beyond which the continuous distribution of atoms around the N atom can be assumed. The parameter, l_0, describes the sharpness of the boundary at r_0. Structure parameters, $n_{N\alpha}$, $l_{N\alpha}$, $r_{N\alpha}$, l_0, and r_0, in Eq. 9 were each determined from the least squares fit. The fitting procedure was performed in the range of $0.3 \leq Q \leq 9.6$ Å^{-1} with the SALS program,[25] under the assumption that the statistical uncertainties distribute uniformly.

The results of the least squares fit for observed $^{0\text{H}}\Delta_N^{\text{inter}}(Q)$ and $a_{\text{NH}}(Q)$ values are shown in Figs. 6a and 6b, respectively. A satisfactory agreement is obtained between observed and calculated structure functions. Corresponding distribution functions, $^{0\text{H}}G_N^{\text{inter}}(r)$ and $g_{\text{NH}}(r)$, are represented in Figs. 7a and 7b, respectively. In the preliminary analysis, the least squares fitting procedures for observed $^{0\text{H}}\Delta_N^{\text{inter}}(Q)$ and $a_{\text{NH}}(Q)$ functions were carried out using the model function involving two Gaussian short-range interactions with a long-range random distribution. However, obtained values of the coordination number for the first nearest neighbor interactions, n_{NO} = 3.0 and n_{NH} = 8.5, were judged to be too large, considering the hydrogen-bonded geometry between the amino group and neighboring water molecules. The first nearest neighbor hydrogen-bonded N···O distance determined from the preliminary analysis, r_{NO} = 2.98 Å, was considered to be exceptionally long when compared with the average value of hydrogen-bonded N(–H)···O distance, 2.89 Å, derived from various organic crystals.[26] Consequently, the final fit was carried out under the assumption that the short-range contributions in both $^{0\text{H}}\Delta_N^{\text{inter}}(Q)$ and $a_{\text{NH}}(Q)$ functions consist of three components.

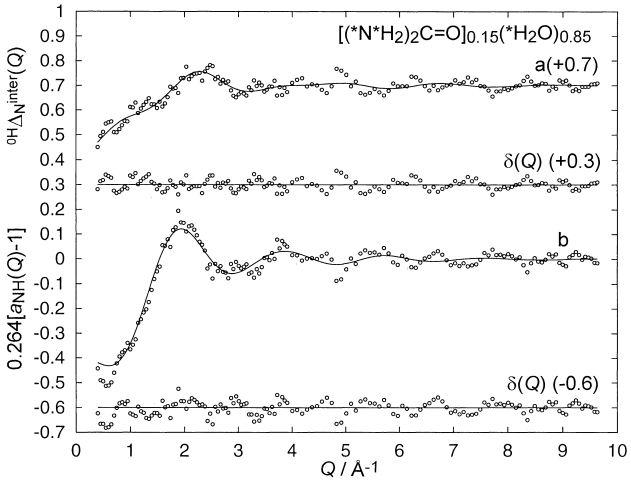

Fig. 6. Circles: Observed a) $^{0\text{H}}\Delta_N^{\text{inter}}(Q)$ and b) $a_{\text{NH}}(Q)$ for the aqueous 15 mol% urea solution. Solid lines: The best-fit of calculated interference terms in Eq. 9. The difference between observed and calculated interference functions, $\delta(Q)$, is given below.

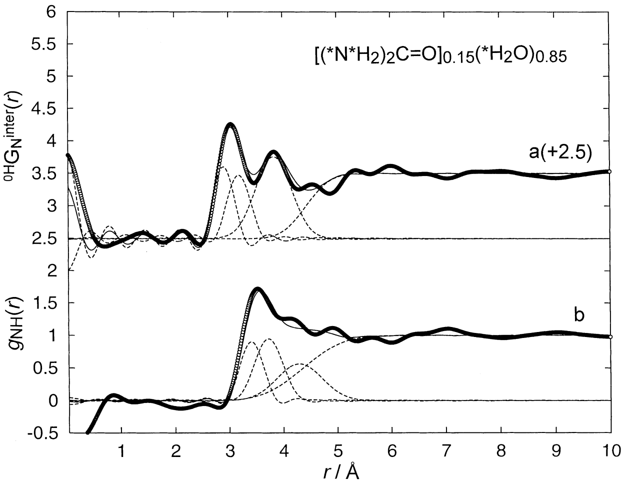

Fig. 7. Circles: Observed a) $^{0\text{H}}G_N^{\text{inter}}(r)$ and b) $g_{\text{NH}}(r)$ for the aqueous 15 mol% urea solution. Solid lines: Fourier transform of the best-fit of calculated interference terms shown in Fig. 6. Short- and long-range components are shown by broken lines.

Final values of all independent parameters are summarized in Tables 3 and 4. The present value of the first nearest neighbor N···O distance, r_{NO} = 2.92(1) Å, agrees well with that observed for the concentrated aqueous $^*\text{N}^*\text{H}_4\text{Cl}$ solution (r_{NO} = 2.87(1) Å)[27] and with those for aqueous glycine solutions in neutral (r_{NO} = 2.85(5) Å),[28] alkaline (r_{NO} = 2.93(3) Å),[29] and acidic (r_{NO} = 2.90(2) Å)[30] conditions. The present coordination numbers for the first nearest neighbor N···O and N···H in-

Table 3. Results of the Least Squares Refinement for the $^{0\text{H}}\Delta_N(Q)$ Observed for the Aqueous 15 mol% Urea Solution[a]

Interaction	i···j	r_{ij}/Å	l_{ij}/Å	n_{ij}
Short-range	N···O(I)[b]	2.92(1)	0.12(2)	2.0(1)
	N···O(II)[c]	3.20(2)	0.18(3)	2.6(5)
	N···O*(III)[d]	3.86(3)	0.33(3)	8.4(3)
	i···j	r_0/Å	l_0/Å	
Long-range	N···X[e]	4.46(1)	0.36(1)	

a) Estimated standard deviations are given in parentheses. b) The first nearest neighbor N···O interaction. c) The second nearest neighbor N···O interaction. d) The third nearest neighbor N···O interaction that may involve N···N interaction. e) X: O, C and N.

Table 4. Results of the Least Squares Refinement for the $a_{NH}(Q)$ Observed for the Aqueous 15 mol% Urea Solution[a)]

Interaction	i···j	r_{ij}/Å	l_{ij}/Å	n_{ij}
Short-range	N···H(I)[b)]	3.42(1)	0.18(2)	4.1(2)
	N···H(II)[c)]	3.74(2)	0.25(3)	6.6(5)
	N···H(III)[d)]	4.34(1)	0.41(2)	8.6(2)
	i···j	r_0/Å	l_0/Å	
Long-range	N···H	4.44(1)	0.58(1)	

a) Estimated standard deviations are given in parentheses. b) The first nearest neighbor N···H interaction. c) The second nearest neighbor N···H interaction. d) The third nearest neighbor N···H interaction.

teractions, $n_{NO} = 2.0(1)$ and $n_{NH} = 4.1(2)$, are consistent with the expected structure where each amino-hydrogen atom forms hydrogen bonds of the N–H···OH$_2$ type. The tilt angle between the N–H···O axis and the molecular plane of the hydrogen-bonded water molecule is estimated to be 51(5)°, employing the known molecular structure of D_2O in the liquid state determined by neutron diffraction study ($r_{OD} = 0.983$ Å, $r_{DD} = 1.55$ Å).[31] The number of the second nearest neighbor water molecules around the amino nitrogen atom is determined to be ca. 3, suggesting strong hydration of the amino group. It is considered that significant amounts of water molecules in the solution are mobilized to the hydration shell around the amino group. This leads to a considerable modification of the hydrogen-bonded network structure among solvent water molecules. The present value of the second nearest neighbor N···O(II) distance (3.20 Å) is much shorter when compared with that for the non-hydrogen bonded O···O interaction (ca. 3.4 Å) which has often been found in pure water[15,32] and aqueous solutions.[33] It may be considered that the contribution from water molecules hydrogen-bonded to the neighboring urea molecule is involved in the present N···O(II) interaction. The third nearest neighbor N···O interaction may involve water molecules within the first hydration shell of both carbonyl and other amino groups of the urea molecule. In order to obtain more detailed structural information concerning both the hydration shell around the carbonyl group and the hydrogen bonds among solvent water molecules, knowledge of partial structure factors, $a_{HH}(Q)$, $a_{OH}(Q)$ and $a_{OO}(Q)$, may be important. This would require an additional measurement on "$^{0-2}H_2O$" solution with the average scattering length of the hydrogen atom being $(b_D + b_{^0H})/2$. Along this line, neutron diffraction measurements and data analysis are now in progress.

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