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The excluded volume effect in confined fluids and liquid mixtures

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Abstract. It is shown that unless excluded volume effects are included in the comparison between solution and pure liquid radial distribution functions, the conclusion that a particular solute either enhances, decreases or has no effect on solvent structure may be erroneous. The effect is most pronounced when the ratio between the volume occupied by the solute molecules or ions and that occupied by the solvent molecules approaches unity. The case of acetylcholine in aqueous solution is analysed as an example.

1. Introduction

The advent of the ISIS high-flux pulsed neutron source means that it is becoming increasingly feasible to explore, by neutron diffraction and isotope substitution, the structure of relatively complex liquid mixtures and solutions. In many cases, by a suitable combination of diffraction data from different isotopic compositions, specific atom–atom radial distribution functions, $g(r)$, can be extracted. Perhaps the most common distributions are those of the solvent hydrogen to solvent hydrogen (HH) and solvent hydrogen to other atom (XH) radial distribution functions in confined fluids and liquid solutions (Soper and Turner 1993). At the same time numerous computer simulations of solutions and fluid mixtures are available, and these too produce radial distribution functions as one of their primary results.

Often one of the tasks is to establish the extent to which the solvent structure in these cases has changed in the presence of dissolved molecules and ions compared to the pure liquid. Since the radial distribution functions are the primary result of a diffraction experiment and are also widely reported in computer simulations, it is natural to compare the radial distribution functions of the solvent in the solution with the radial distribution functions of the solvent on its own. In the neutron experiment this is especially true of the solvent HH distribution which can often be obtained free from solute–solute and solute–solvent contributions, but for the computer simulation all solvent–solvent site–site radial distribution functions are available, both in the pure solvent and in the solution.

The question that arises however is the following: how do you make that comparison? Do you simply compare the ‘raw’ as-measured radial distribution functions? This is in fact what has traditionally been done, and as a consequence statements have been made that the solvent is more or less structured in the presence of a particular solvent. To understand what might happen in this case, however, consider a simple thought experiment. Figure 1(a) shows a single sphere of radius R containing an ideal gas and sitting in an otherwise empty space. The atoms of this gas are distributed randomly and uniformly within the sphere, but

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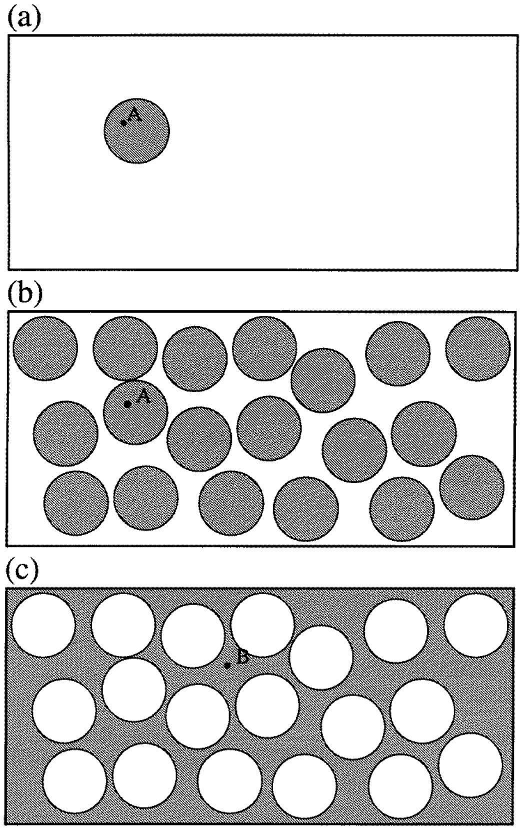

Figure 1. (a) The case of a single finite-sized molecule in space containing an ideal gas. Starting from the point A, the local density near this point, when averaged over all directions, is equal to the density of the gas. Far away however the density is zero, due to the confinement of the gas. (b) An ensemble of particles of the kind shown in (a). Again starting from point A the local average density is equal to the density of the gas. Far away from A the average density is lower due to the volume of gas excluded from the space between particles, but it is not zero. (c) This is the inverse of (b): now the fluid is only allowed in the space *between* the particles. This is the case encountered when attempting to compare the structure of water in a solution with that in the pure liquid. The local density of water near point B is higher than the average water density in the system.

do not exist outside it. Starting from any particular atom (e.g. point A in figure 1(a)) the radial distribution function will be unity in the immediate vicinity of the atom, but must decay to zero for $r > 2R$, since that is the maximum distance that any two atoms can occur at. The radial distribution function is straightforward to calculate in this case, and can be shown to be (Glatter and Kratky 1992)

$$g_p(r) = \begin{cases} 1 - \frac{3}{4}(r/R) + \frac{1}{16}(r/R)^3 & \text{for } r \leqslant 2R \\ 0 & \text{for } r > 2R. \end{cases} \tag{1}$$

The suffix p here is to indicate that this is the radial distribution function for a single particle. We note at this stage that although the gas contained in the sphere is ideal, for which normally $g_p(r) = 1$ for all r, the fact that it is confined perturbs the expected radial

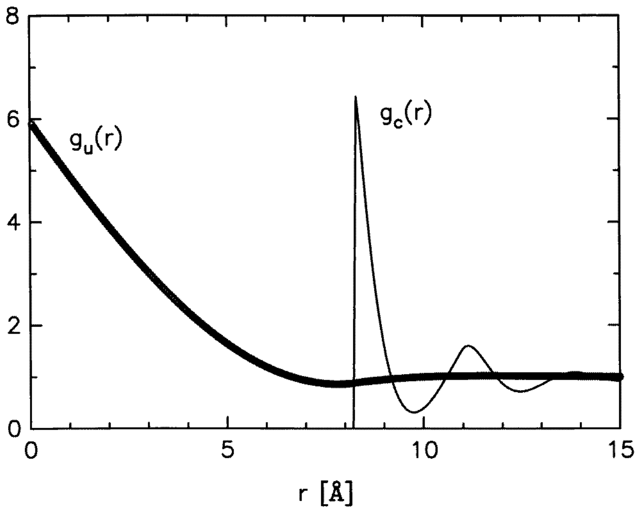

Figure 2. Comparison of the centre radial distribution function for a fluid of hard-sphere solute molecules of diameter 8.28 Å in a solvent made up of spheres of diameter 2.7 Å, in the ratio of one solute molecule to 50 solvent molecules (line), with the convoluted radial distribution function (equation (14), circles) corresponding to the confined uniform fluid.

behaviour. However this effect has nothing to do with any altered interaction between the gas atoms themselves, which are still ideal gas atoms. It has only to do with the enforced confinement.

Now consider what happens when there is an assembly of such particles (figure 1(b)). For convenience the particles are assumed to be spherical, identical and non-overlapping, but this does not affect the underlying argument. Clearly the particles will have a distribution of centres, $g_c(r)$, which is distinct from the internal radial distribution, $g_p(r)$. Figure 2 (thin line) shows a typical hard-sphere centre radial distribution function, obtained from the Percus–Yevick equation. The total radial distribution function of this system will therefore be a convolution of this centre distribution with the individual particle $g_p(r)$ radial distribution function (see the next section), and this is shown as the thick line in figure 2. Note that in performing this convolution a new term, namely the $\delta(\boldsymbol{r})$ function corresponding to the particle correlating with itself, which is not normally plotted in graphs of $g(r)$, has now appeared, because the finite extent of each particle means that this *self-radial distribution* is now visible. We note that as a result of this extra term $g(r)$ now goes to unity at large r as expected but is significantly *above* unity in the low-r region. Physically this has a simple explanation in that with the coordinate origin on one atom inside a particle that atom will ‘see’ a local number density which is significantly higher than the average atomic number density of the system, which is diluted by the fact that atoms are *excluded* from regions between the spherical particles. Hence the term *excluded volume effect* is used to describe this result.

Finally, the case of most relevance to the present context, of solvent correlations in the presence of a solute, is that when the atoms are allowed everywhere *except* inside the particles (figure 1(c)) with the ideal gas atoms being regarded as the solvent, and the spherical particles as the solute. In fact this case is the exact inverse of case (b), and apart from a constant has the same form for the solvent radial distribution function, as will be seen below. Inspection of figure 2 therefore already shows that the excluded volume effect on the solvent radial distribution functions will be most significant in cases where the near-neighbour separation of the solvent atoms is less than a typical diameter of the solute particles.

In the rest of this paper, the underlying formalism that accompanies this verbal summary for case (b) is described in section 2, while the extension of this to the excluded volume correction for the HH, XH and XX radial distribution functions in aqueous solutions (case (c)) is described in section 3. Finally there is a brief discussion and conclusion in section 4.

2. Theory of the excluded volume effect

The quantity obtained in a diffraction experiment is the static structure factor, $S(Q)$, which is related by Fourier transform to the static ($t = 0$) van Hove autocorrelation function, $G(r)$ (Hansen and Macdonald 1986)

$$G(\boldsymbol{r}) = \frac{1}{N} \int \langle n(\boldsymbol{r}') n(\boldsymbol{r}' + \boldsymbol{r}) \rangle \, \mathrm{d}\boldsymbol{r}' \tag{2}$$

where N is the number of point particles in the system of volume V, and the instantaneous local particle number density at position $\boldsymbol{r}$ is defined as

$$n(\boldsymbol{r}) = \sum_{j}^{N} \delta(\boldsymbol{r} - \boldsymbol{R}_j) \tag{3}$$

with $\boldsymbol{R}_j$ the position of the jth particle. The angle brackets in (2) denote a statistical average of this correlation function over the accessible energy states of the system. Substituting (3) into (2) we find

$$G(\boldsymbol{r}) = \delta(\boldsymbol{r}) + \frac{1}{N} \left\langle \sum_{j \neq i} \delta(\boldsymbol{r} - \boldsymbol{R}_i + \boldsymbol{R}_j) \right\rangle = \delta(\boldsymbol{r}) + \bar{n} g(r) \tag{4}$$

where $\bar{n} = N/V$ is the average number density of particles and $g(r)$ is the radial distribution function of particles. It is this latter function ('distinct' term) that is normally reported in diffraction experiments and computer simulations of fluids, even though the preceding $\delta(\boldsymbol{r})$ function ('self'-term), which corresponds to the particle correlating with itself (and which spreads out in space for $t > 0$), is also measured.

If the particles have a finite size and shape they will be here called molecules, and it is necessary to distinguish between the distribution of molecular *centres* (denoted by the subscript c) and the internal distribution of atomic density within the molecules and relative to the centre (denoted here by the subscript p). Writing N_c for the number of molecular centres in a system of volume V, and $\bar{n}_c$ for the number density of centres, the centres autocorrelation function $G_c(\boldsymbol{r})$ can be written immediately from (2) and (4) as

$$G_c(r) = \frac{1}{N} \int \langle n_c(\boldsymbol{r}') n_c(\boldsymbol{r}' + \boldsymbol{r}) \rangle \, \mathrm{d}\boldsymbol{r}' = \delta(\boldsymbol{r}) + \bar{n}_c g_c(r) \tag{5}$$

where $g_c(r)$ is the radial distribution function for molecular centres.

For the case where the molecules are extended and consist of M component atoms located in a molecule fixed frame at positions $\boldsymbol{d}_\mu$, $\mu = 1, \ldots, M$, with respect to the centre of mass, the local atomic number density in an isotropic phase is then given by a sum over the positions of all atoms, as well as an average over the orientations Ω_j of the molecules:

$$n(\boldsymbol{r}) = \frac{1}{(8\pi^2)^{N_c}} \sum_j \sum_\mu \int \{\mathrm{d}\Omega_j\} \delta(\boldsymbol{r} - \boldsymbol{r}_{j\mu}(\Omega_j)) \tag{6}$$

where the position $\boldsymbol{r}_{j\mu}(\Omega_j)$ of the μth atom on molecule j is given by

$$\boldsymbol{r}_{j\mu}(\Omega_j) = \boldsymbol{R}_j + \mathcal{R}(\Omega_j)\boldsymbol{d}_\mu$$

with $\mathcal{R}(\Omega_j)$ a Cartesian rotation that transforms the molecular vectors into laboratory-frame vectors. A dummy integration is now introduced to separate the centre of mass from the internal coordinates:

$$\begin{aligned} n(\boldsymbol{r}) &= \frac{1}{(8\pi^2)^{N_c}} \sum_j \sum_\mu \int \{\mathrm{d}\Omega_j\} \delta(\boldsymbol{r} - \boldsymbol{R}_j - \mathcal{R}(\Omega_j)\boldsymbol{d}_\mu) \\ &= \int \mathrm{d}\boldsymbol{r}' \sum_j \delta(\boldsymbol{r}' - \boldsymbol{R}_j) \frac{1}{(8\pi^2)^{N_c}} \int \{\mathrm{d}\Omega_j\} \sum_\mu \delta(\boldsymbol{r} - \boldsymbol{r}' - \mathcal{R}(\Omega_j)\boldsymbol{d}_\mu) \\ &= \int \mathrm{d}\boldsymbol{r}'\, n_c(\boldsymbol{r}') n_p(\boldsymbol{r} - \boldsymbol{r}') \end{aligned} \tag{7}$$

which serves to define the internal atomic density distribution $n_p(\boldsymbol{r})$ of a molecule: this function goes to zero outside the molecule. For example in an x-ray experiment $n_p(\boldsymbol{r})$ might be the electron density distribution of a molecule, while for neutron scattering it would be the neutron scattering length density distribution.

This atomic density distribution (7) is now substituted into the autocorrelation function (4) as before. However if the particles are not spherically isotropic, there is a complication in doing this in that the internal density distribution $n_p(\boldsymbol{r})$ is dependent on the *orientation* of each molecule. This means that different results will be obtained for the self- and distinct terms. However for the present purposes, and in line with the discussion given in the introduction, it is sufficient to assume that orientational correlations between distinct molecules are weak so that for the distinct term the orientational averages can be performed as if the molecules were uncorrelated. For the practical cases in which excluded volume effects are significant, this is a satisfactory approximation.

With this approximation the result is

$$\begin{aligned} G(\boldsymbol{r}) &= \frac{1}{N} \left\langle \int \mathrm{d}\boldsymbol{r}'\, n(\boldsymbol{r}') n(\boldsymbol{r}' + \boldsymbol{r}) \right\rangle \\ &= \frac{1}{N} \int \mathrm{d}\boldsymbol{r}' \int \mathrm{d}\boldsymbol{r}'' \int \mathrm{d}\boldsymbol{r}'''\, \langle n_c(\boldsymbol{r}'') n_c(\boldsymbol{r}''') \rangle \langle n_p(\boldsymbol{r}' - \boldsymbol{r}'') n_p(\boldsymbol{r}' + \boldsymbol{r} - \boldsymbol{r}''') \rangle_\Omega \end{aligned} \tag{8}$$

where $N = MN_\mathrm{c}$. With the substitution $\boldsymbol{u} = \boldsymbol{r}'' + \boldsymbol{r} - \boldsymbol{r}'''$, and $\boldsymbol{u}' = \boldsymbol{r}' - \boldsymbol{r}''$, equation (8) can be rewritten

$$G(\boldsymbol{r}) = \frac{1}{N} \int \mathrm{d}\boldsymbol{u} \int \mathrm{d}\boldsymbol{r}'' \langle n_c(\boldsymbol{r}'') n_c(\boldsymbol{r}'' + \boldsymbol{r} - \boldsymbol{u}) \rangle \int \mathrm{d}\boldsymbol{u}' \langle n_p(\boldsymbol{u}') n_p(\boldsymbol{u}' + \boldsymbol{u}) \rangle_\Omega. \tag{9}$$

If the single-molecule internal autocorrelation function is written as $G_p^{(s)}(\boldsymbol{u}) = (1/M) \int \mathrm{d}\boldsymbol{u}' \langle n_p(\boldsymbol{u}') n_p(\boldsymbol{u}' + \boldsymbol{u}) \rangle_\Omega$ and the distinct molecule internal autocorrelation function as $G_p^{(d)}(\boldsymbol{u}) = (1/M) \int \mathrm{d}\boldsymbol{u}'\, \langle n_p(\boldsymbol{u}') \rangle_\Omega \langle n_p(\boldsymbol{u}' + \boldsymbol{u}) \rangle_\Omega$, then with (5) we obtain finally

$$\begin{aligned} G(r) &= \int \mathrm{d}\boldsymbol{u}\, \delta(\boldsymbol{r} - \boldsymbol{u}) G_p^{(s)}(\boldsymbol{u}) + \frac{1}{N_c} \sum_{j \neq i} \int \mathrm{d}\boldsymbol{u}\, \delta(\boldsymbol{r} - \boldsymbol{u} - \boldsymbol{R}_i + \boldsymbol{R}_j) G_p^{(d)}(\boldsymbol{u}) \\ &= \bar{n}_p g_p^{(s)}(r) + \bar{n}_p \bar{n}_c \int \mathrm{d}\boldsymbol{u}\, g_c(\boldsymbol{r} - \boldsymbol{u}) g_p^{(d)}(\boldsymbol{u}) \end{aligned} \tag{10}$$

where $\bar{n}_p = M/v_p$ represents the average scattering density *inside* the molecules, v_p represents the nominal volume occupied by an individual molecule, and we have defined the internal radial distribution functions of the molecule as $g_p^{(s)}(\boldsymbol{r}) = (1/\bar{n}_p) G_p^{(s)}(r)$, etc.

Note that if the molecules are spherically isotropic then the self- and distinct terms of these internal radial distribution functions become identical, so the superscripts, (s) and (d), can be dropped in that case.

The autocorrelation function for the system therefore consists of two contributions, namely a single-molecule internal radial distribution term and a second term which is a convolution of the distinct-molecule internal radial distribution function with the molecular centre radial distribution function.

Although this result is straightforward, and probably for the most part obvious, it has an important consequence which is not widely appreciated for scattering experiments and computer simulations on aqueous solutions containing large molecules, or in systems where a fluid is confined within a porous structure. As a simple example suppose, as in the introduction, the system consists of hard core molecules or pores of radius R, containing ideal gas atoms. The density inside each molecule is continuous and uniform out to the edge of the molecule, i.e.

$$n_p(\boldsymbol{r}) = \begin{cases} \bar{n}_p & \text{for } |\boldsymbol{r}| \leqslant R \\ 0 & \text{for } |\boldsymbol{r}| > R. \end{cases} \tag{11}$$

This gives rise to the exact form, equation (1), for the particle internal radial distribution function, $g_p(r)$, and we note that $4\pi \int g_p(r) r^2 \, \mathrm{d}r = v_p$. This form also has an exact Fourier transform to Q space and we define the internal particle structure factor as

$$S_p(Q) = \frac{4\pi}{v_p} \int g_p(r) r^2 \frac{\sin Qr}{Qr} \, \mathrm{d}r = 9 \left[\frac{(\sin QR - QR \cos QR)}{(QR)^3} \right]^2 .$$

If the autocorrelation function is transformed to Q space it enables the convolution in (10) to be performed as a product of Fourier transforms:

$$S(Q) = \int \mathrm{d}\boldsymbol{r}\, G(\boldsymbol{r}) \exp(\mathrm{i}\boldsymbol{Q} \cdot \boldsymbol{r}) = M S_p(Q) + M H_c(Q) S_p(Q) + N_c M \delta(\boldsymbol{Q}) \tag{12}$$

where

$$H_c(Q) = \bar{n}_c \int \mathrm{d}\boldsymbol{r} \exp(\mathrm{i}\boldsymbol{Q} \cdot \boldsymbol{r})[g_c(\boldsymbol{r}) - 1]. \tag{13}$$

Inverse Fourier transformation of (12) then yields the autocorrelation function for the system (10), and, since the results of most experiments are reported as radial distribution functions, it is useful display the radial distribution function associated with equation (10), namely

$$g(\boldsymbol{r}) = \frac{1}{\bar{n}} G(r) = \frac{V}{V_p} g_p^{(s)}(r) + \frac{1}{v_p} \int \mathrm{d}\boldsymbol{u}\, g_c(\boldsymbol{r} - \boldsymbol{u}) g_p^{(d)}(\boldsymbol{u}) \tag{14}$$

where the average scattering density in the system is given by $\bar{n} = M\bar{n}_c$, and $V_p = N_c v_p$ represents the total volume of the system occupied by the molecules. It should be noted that the ratio $V/V_p \equiv \bar{n}_p/\bar{n}$, which can be used to evaluate the effective volume of the molecules in any particular case, provided a reasonable estimate of the average density inside the molecules is available.

Using (14) it is now possible to understand where the excluded volume effect comes from. At $r = 0$, $g_p(r) = 1$, while $g_c(\boldsymbol{r} - \boldsymbol{u}) = 0$ (if the particles do not overlap), so $g(r = 0) = V/V_p$. At large r, however, $g_p(r) = 0$, while $g_c(\boldsymbol{r} - \boldsymbol{u}) = 1$, so $g(r) = 1$ by virtue of the normalization of $g_p(r)$. Since the total volume occupied by the molecules, V_p, is necessarily smaller than the total volume of the system, V, the radial distribution function rises above unity at low r.

As an example of the application of this result we consider the case of hard-core molecules of diameter 8.28 Å at a density of 5.65×10^{-4} molecules per cubic ångström—this corresponds to the concentration in a recent experiment on acetylcholine bromide in solution (1 mol acetylcholine bromide to 50 mol water; Hulme *et al* 1997). The centre structure factor, $H_c(Q)$, was calculated within the Percus–Yevick approximation for a binary mixture of hard spheres (see Lebowitz 1964) and multiplied by the uniform molecule form factor as given in (12). For the purpose of this calculation it was assumed the water molecules could be also be represented by hard-core molecules of diameter 2.7 Å, corresponding to the likely near-neighbour approach of water molecules. The densities of both components were kept to their experimental values, which gives a packing fraction of 0.45—a density region where the Percus–Yevick approximation starts to break down (Hansen and Macdonald 1986), but nonetheless gives useful results beyond the hard-core radius of the particles. Finally the resulting total structure factor was transformed numerically back to r space, and the result is shown in figure 2.

It can be seen that the result of the convolution, (10), is drastically altered compared to the original centre radial distribution function. In particular the central $\delta(\boldsymbol{r})$ function in the centre autocorrelation function, which cannot be plotted, spreads out to a broad distribution out to 8 Å in the radial distribution function. Moreover, the place where the edge of the centre distribution occurs, also at $r = 8.28$ Å, is now close to the first *minimum* in the convoluted $g(r)$.

The centres radial distribution function in this case is dominated by the smaller water molecules. According to the present analysis with the Percus–Yevick approximation, the hard-core edge of the centres radial distribution function occurs at 8.28 Å as expected, but the subsequent oscillations in the centres function have a period closer to that of the smaller water molecules. Very likely the acetylcholine centre distribution in the real solution will not look like this at all, since the acetylcholine molecules are certainly not spherical, nor can water be modelled with a hard-core interaction, but in the convoluted $g(r)$ it will be seen that the inter-molecular correlation between solute particles has been largely washed out by the convolution, in spite of the large amount of structure in the centres function. Therefore the results of the analysis are to a very good approximation *independent* of the precise details of the centres function.

Another distinctive feature of the convoluted $g(r)$ is that at low r the radial distribution function rises considerably above the large-r limit of unity. This rise is generated by the factor V/V_p outside the first term in equation (14), which in this example has the value of 5.95. The change in level of $g(r)$ from low to high r arises from the change in the local density, from $\bar{n}_p$ at low r to $\bar{n}$ at high r. A recent example of a system where this effect was seen was the measurement of water structure in porous ionomer membranes (Lee *et al* 1992): the water in this case was confined to roughly spherical pores of radius ~ 18 Å. Other examples include the case of fluids such as helium in Vycor glass.

In the analysis so far the fluid has been confined but has no intrinsic structure of its own. For clarity the radial distribution function for this uniform fluid is labelled $g_u(r)$ to distinguish it from the case of what might be observed if it were a real fluid. In fact if this were a real fluid it would have a structure in its own right, which would be signalled as peaks in the molecule internal radial distribution function, $g_p^{(s)}(r)$. The point to be made here is that when analysing the structure of the liquid the amplitudes of the oscillations in $g(r)$ are compared against the radial distribution function for a system where there are no interactions between the atoms. This latter distribution function is a flat line for a homogeneous system, but for a heterogeneous system where the atoms cannot occupy all of space, and where the scale of the confinement is significantly greater than the size of individual atoms, this so-called uncorrelated distribution function develops a structure of its own precisely by virtue of the confinement of the atoms. Any radial distribution function for the liquid in the confined system must be corrected for this structure if it is to be compared to the distribution function of the same *unconfined* liquid.

The basic proposal of this paper is that in order to compare the structure of the same fluid in different environments, such as in confined geometry, or in solution, the raw radial distribution function, $g(r)$, obtained by Fourier transformation of the diffraction data, or derived by computer simulation, should not be used for this purpose, but instead a renormalized radial distribution function should be generated, defined by dividing the radial distribution function by the uniform fluid radial distribution function for the particular environment concerned:

$$\tilde{g}(r) = g(r)/g_u(r). \tag{15}$$

This would allow the most accurate comparison of the fluid structures in the two environments.

The analysis so far applies to the case of a fluid confined in a porous material, that is, the case of figure 1(b). Therefore the next section addresses the question of how the uniform fluid radial distribution function might be calculated in the other common situation, that is, when the fluid is *excluded* from certain regions of the sample, which is the case shown in figure 1(c). In fact this requires only a minor extension to the analysis. This is the case most frequently encountered in aqueous solution studies.

3. Application to aqueous solution neutron scattering studies

By employing hydrogen–deuterium substitution on an aqueous solution, one can obtain from neutron diffraction with three isotopic contrasts three composite partial radial distribution functions, namely HH, HX and XX, where H represents the protons on which a substitution is made, and X represents a weighted sum of all non-substituted atoms (Soper and Turner 1993). If the protons substituted correspond to the water or exchangeable hydroxyl protons, then every place where a solute molecule or ion occurs must by definition exclude water from that region. In other words there will be a hole in the substituted proton distribution in the vicinity of the molecule. This situation, which is essentially the mirror image of the case at the end of the previous section, can be dealt with by a simple extension of the previous analysis.

3.1. The uniform-fluid radial distribution function for the HH correlations

In this instance the problem can be treated as a bulk uniform fluid in which holes are created by the dissolved molecules. Thus the uniform-fluid hydrogen distribution function can be written down from (7) as

$$n_H(\boldsymbol{r}) = n_H - \int \mathrm{d}\boldsymbol{r}'\, n_c(\boldsymbol{r}') n_p^{(H)}(\boldsymbol{r} - \boldsymbol{r}') \tag{16}$$

where $n_p^{(H)}(\boldsymbol{r})$ is defined by (11) with $\bar{n}_p^{(H)} = n_H$, and n_H is typically the hydrogen atom number density of the bulk fluid: it is strictly the hydrogen density that occurs in regions not occupied by solute molecules. The average hydrogen density in the system is therefore

$$\bar{n}_H = \frac{1}{V} \int \mathrm{d}\boldsymbol{r}\, n_H(\boldsymbol{r}) = n_H \left[1 - \frac{V_p}{V}\right]. \tag{17}$$

Using (16) in (9), with (10) and (14), to calculate the uniform fluid radial distribution function as before, new terms appear:

$$g_u^{(HH)}(r) = \left(1 - \frac{V_p}{V}\right)^{-2} \left[1 - 2\frac{V_p}{V} + \frac{V_p}{V} g_p^{(HH)}(r) + \left(\frac{V_p}{V}\right)^2 \frac{1}{v_p} \int \mathrm{d}\boldsymbol{u}\, g_c(\boldsymbol{r} - \boldsymbol{u}) g_p^{(HH)}(\boldsymbol{u})\right]. \tag{18}$$

It is now seen that in the limit of $r = 0$ $g_u^{(HH)}(r) \approx (1 - V_p/V)^{-1}$, i.e. it goes *above* unity at low r by an amount which is inversely proportional to the relative volume of solvent in the solution compared to the total volume of fluid present, while at large r $g_u^{(HH)}(r) \approx 1$ as expected.

For the case of acetylcholine discussed in the previous section the density of water protons is 0.0556 H atoms Å^{-3} compared to the value of 0.0668 Å^{-3} in pure water. This means the product $\bar{n}_c v_p = 1 - \bar{n}_H / n_H \approx 0.168$, so, since $\bar{n}_c \approx 0.000\,565$ Å^{-3} for this case, $v_p = 297.3$ Å^{-3}, which gives an effective molecule radius of 4.14 Å. This is the origin of the numbers used in the previous section. Using the same procedure as defined in the previous section, these numbers can be used to estimate $g_u^{(HH)}(\boldsymbol{r})$.

Comparison of this calculation with the actual measured $g_{HH}(r)$ function for this system is shown in figure 3(a): it is clear that the measured HH radial distribution function does indeed show the predicted positive deviation at low r, and that assuming the acetylcholine molecule is spherical for the purpose of calculating the excluded volume effect gives a reasonable account of this deviation.

Finally the measured data can be renormalized to the uniform fluid, as suggested in (15) above. The result, shown in figure 3(b), now shows excellent agreement with the pure water data, and indicates that water structure is not discernibly perturbed by the presence of acetylcholine at this concentration. The above procedure can therefore be used reliably to assess the extent to which excluded volume effects will modify any conclusions that are to be drawn about the modification of the solvent structure by a solute.

3.2. XX and XH composite radial distribution functions

Given the result of subsection 3.1, it is now straightforward to generate the equivalent uniform-fluid approximation for the other radial distribution functions. For the unlabelled X molecules the density will not necessarily drop to zero inside the solute molecules, but will in general be different from the solvent. Thus

$$n_X(\boldsymbol{r}) = n_X + \int \mathrm{d}\boldsymbol{r}' n_c(\boldsymbol{r}') n_p^{(X)}(\boldsymbol{r} - \boldsymbol{r}') \tag{19}$$

where n_X is the scattering density of X atoms in the solvent region of the fluid and $\bar{n}_p^{(X)} = (1 + f_s) n_X$ is the scattering density of X atoms inside the solute molecules. Then the average density of X atoms is $\bar{n}_X = n_X[1 + f_s V_p / V]$ while the uniform-fluid radial distribution functions are

$$g_u^{(XX)}(r) = \left(1 + f_s \frac{V_p}{V}\right)^{-2} \left[1 + 2 f_s \frac{V_p}{V} + f_s^2 \frac{V_p}{V} g_p^{(XX)}(r) \right.$$
$$\left. + \left(f_s \frac{V_p}{V}\right)^2 \frac{1}{v_p} \int \mathrm{d}\boldsymbol{u}\, g_c(\boldsymbol{r} - \boldsymbol{u}) g_p^{(XX)}(\boldsymbol{u})\right] \tag{20}$$

and

$$g_u^{(XH)}(r) = \left[\left(1 + f_s \frac{V_p}{V}\right)\left(1 - \frac{V_p}{V}\right)\right]^{-1} \left[1 + (f_s - 1)\frac{V_p}{V} - f_s \frac{V_p}{V} g_p^{(XH)}(r)\right.$$

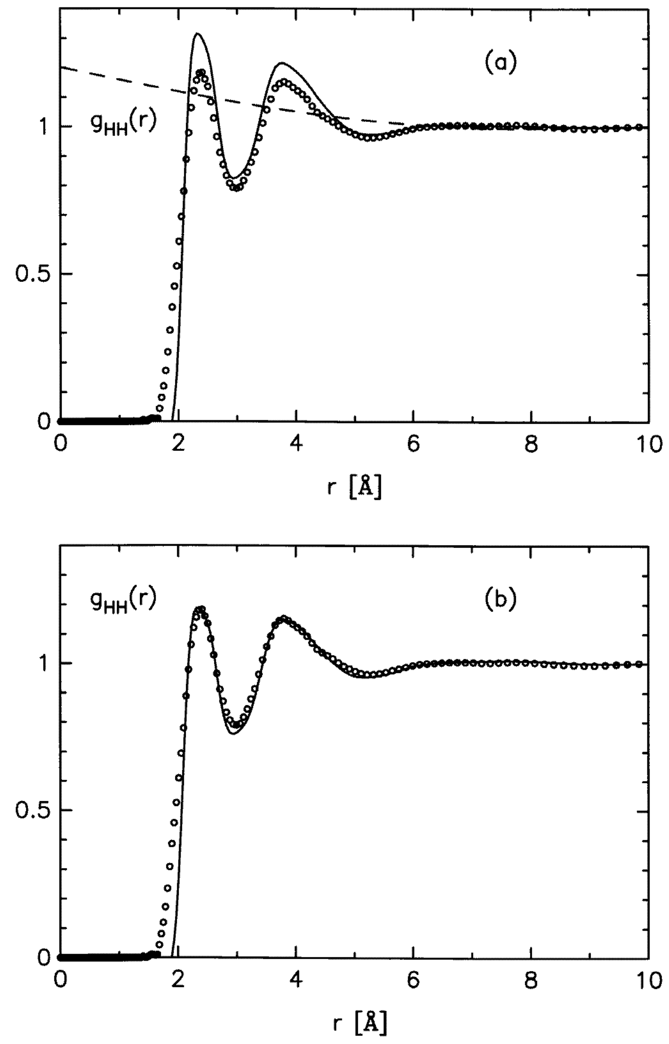

Figure 3. (a) The measured HH pair radial distribution function for acetylcholine solutions (line) compared to the same function for pure water (circles). The dashed line shows the excluded volume effect for the water protons in the acetylcholine solution (equation (18)). (b) The renormalized HH pair radial distribution function for acetylcholine solution which takes account of the excluded volume effect (line), compared with the same function for pure water (circles). Note that the effect of the renormalization is to show there is no significant enhancement of the water structure at this concentration even though direct comparison of the measured data (figure 2(a)) might suggest that such an enhanced structure in solution is actually occurring.

$$-f_s\left(\frac{V_p}{V}\right)^2\frac{1}{v_p}\int \mathrm{d}\boldsymbol{u}\, g_c(\boldsymbol{r}-\boldsymbol{u})g_p^{(XH)}(\boldsymbol{u})\Bigg]. \tag{21}$$

Note that both forms have the correct limiting behaviour at large r, while the low-r limits are $[1+2f_sV_p/V+f_s^2V_p/V]/(1+f_sV_p/V)^2$ for XX and $1/(1+f_sV_p/V)$ for XH. In particular it will be noted that the XX radial distribution function is always above unity at low r for all f_s (other than zero), while the XH radial distribution function is below unity if $f_s > 0$.

It is worth noting that the intra-solute density functions $n_p^{(H)}(\boldsymbol{r})$ and $n_p^{(X)}(\boldsymbol{r})$ and the three radial distribution functions associated with them, $g_p^{(HH)}(\boldsymbol{r})$, $g_p^{(XH)}(\boldsymbol{r})$ and $g_p^{(XX)}(\boldsymbol{r})$, will not be identical in general, because for the H distribution the density will normally be uniformly zero inside the solute molecule, providing there is no solvent penetration, while the X distribution may contain some residual structure, depending on the placing of the atoms in the solute particle. For illustrative purposes however it is sufficient to treat them as having a uniform internal density distribution.

4. Discussion and conclusion

The formulae of the preceding sections demonstrate the importance of taking account of the excluded volume effect when comparing radial distribution functions from the same solvent in different systems. Two significant approximations have been made in doing this, namely assuming the solute particle has no internal structure, and also assuming that the solute particle can be represented by a spherically isotropic distribution function. The former assertion is exactly true for the HH function, when the solvent is completely excluded from the solute, since the autocorrelation in this case function is sampling the uniform *absence* of H scattering density inside the solute particle. In fact the HH function is the most useful for comparing the solvent structure in different environments, since it can often be measured independently from any other correlation function in the system. It will also apply to the fluid in pores situation, since again the particle radial distribution function is simply measuring the regions where fluid is allowed and can have no internal structure. In these situations the particle radial distribution function $g_p(r)$ samples the *shape* of the cavity confining the fluid or created by the solute molecule, but is not sampling its internal structure. For the XX and XH functions, and in fact in all situations when the factor $f_s \neq -1$, it will be necessary in general to introduce some structure into the solute molecule, via the internal particle radial distribution functions, $g_p^{(XH)}(\boldsymbol{r})$ and $g_p^{(XX)}(\boldsymbol{r})$.

The assumption that the solute molecule can be represented by an effective spherically isotropic distribution is equally an approximation which may need to be tested in individual cases, but in the majority of situations where excluded volume effects are significant, namely when the solute molecules or cavities are significantly larger than the solvent molecules, it is reasonable, since in those cases the orientation of the solute molecule will not normally be strongly correlated with the orientations of the solvent molecules. Of course the assumption of hard-core particles is less satisfactory for real systems, since in practice the edges of a real solute molecule cavity will be blurred when viewed from the centre of the cavity or molecule. This again will not affect the qualitative results shown in figures 2 and 3—the effect of blurred edge to a particle will appear primarily in the large-r tail of $g_p(r)$, rather than having any strong effect at lower r.

There have been several instances (Franks and Desnoyers 1985, Ferrario *et al* 1990, Soper and Luzar 1992, Turner and Soper 1994) where changes to the water–water correlations in computer simulations and neutron scattering experiments on aqueous solutions have been noted. Often it is found there is a roughly linear increase in the height of say the first O–O peak with increasing concentration (Ferrario *et al* 1990). However, since excluded volume effects are rarely if ever taken into account, it is not clear what is the significance of these increases. According to equation (18) the increase of the local density at low r is inversely proportional to the relative volume of solvent in the fluid. Since this volume decreases with increasing solute concentration, an increase in the height of the water–water correlations at low r as the concentration increases is not at all unexpected. It cannot be taken to automatically imply that the water has somehow enhanced its structure in the presence of the solute. Only after excluded volume effects are accounted for, for example by generating a renormalized radial distribution function such as equation (15), can comments about changes to the solvent structure be made. By the same token the apparent absence of changes to the solvent structure in solution (Turner and Soper 1994) cannot be assumed to indicate that such changes are truly absent, unless the excluded volume effect is estimated and shown to be small.

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