

# Isotopic Substitution Techniques in Disordered Materials Experiments

The use of isotopic samples in Disordered Materials experiments is extremely common, important, and powerful. “Isotopic labelling” or “isotopic substitution” permits the maximal amount of data to be obtained from neutron diffraction experiments – since the focus is usually on hydrogen, you will often hear this referred to simply as “deuteration”, which is the replacement of hydrogen atoms with their heavier isotope, deuterium.

We outline herein the ideas behind isotopic substitution experiments, and list some useful sets of isotope measurements to apply in Disordered Materials experiments.

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## 1 Why do we need isotopic substitution?

It is straightforward to make a neutron measurement on a system, but no matter how complex the system is in terms of the number of different components (e.g. molecules, ions, crystallites, proteins etc.) the end output is the same – a single curve containing information on all correlations between these components, otherwise known as the *structure factor*. There is simply not enough information in this single curve to be able to extract an unambiguous set of correlation functions between components, which is typically what we are interested in doing.

We can think of the total structure factor, or  $F(Q)$ , as a weighted sum of all the partial structure factors between the different atom types in the system, indicated by  $i$  and  $j$ :

$$F(Q) = \sum_{i,j} (2 - \delta_{ij}) c_i c_j b_i b_j S_{ij}(Q) \quad (1)$$

To dissect each part of this equation in turn:

- $c_i$  and  $c_j$  are the atomic fractions of atom types  $i$  and  $j$  in the system
- $b_i$  and  $b_j$  are the bound coherent scattering lengths<sup>i</sup> of types  $i$  and  $j$
- $S_{ij}(Q)$  is the partial structure factor between atom types  $i$  and  $j$ , and is related to the Fourier transform of the radial distribution function between those atom types
- $(2 - \delta_{ij})$  counts terms once where  $i = j$  and twice otherwise, and allows the sum to be constructed efficiently

Let us take a moment to understand exactly what we mean by an “atom type”. For water, there are two “types” of atom – oxygen and hydrogen. For methanol, there could be three – oxygen, carbon, and hydrogen – or we could distinguish between the hydrogens on the carbon and the oxygen to get four – oxygen, carbon, H<sub>carbon</sub>, and H<sub>oxygen</sub>. Regardless, the weighted combination of the partial structure factors between all the different possible combinations of atom types gives rise to the total structure factor. Most importantly, the weighting of the partial structure factors involves the bound coherent scattering lengths of the individual atom types, which are dependent on the isotope of the atom type.

Consider good old water as an example – we have two atom types, which are the water oxygen and the water hydrogen. O makes up one third of all atoms in the system, so  $c_O = 1/3$ , and H makes up two thirds, so  $c_H = 2/3$ . Assuming “off the shelf”, natural chemical abundances of the two elements ( $b_O = 0.5804$  fm and  $b_H = -0.3741$  fm) we can then write the weighting factors,  $w_{ij}$  for all three *unique* partial structure factors occurring in the system:

$i$	$j$	$c_i$	$c_j$	$b_i, \text{fm}$	$b_j, \text{fm}$	$c_i c_j b_i b_j = w_{ij}, \text{fm}^2$
O	O	1/3	1/3	0.5804	0.5804	0.0374
O	H	1/3	2/3	0.5804	-0.3741	-0.0482
H	H	2/3	2/3	-0.3741	-0.3741	0.0622

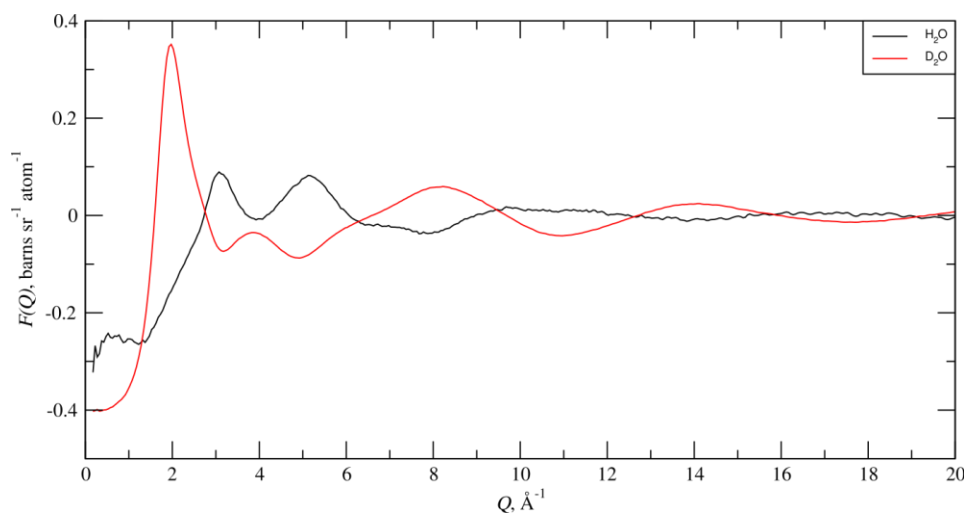
So these are the three “atomic” correlation functions and their respective contributions to the total structure factor, yet even in this simple “two component” (H and O) case, we cannot unambiguously work backwards from the measured  $F(Q)$  and extract these individual partials, since there is not enough information to work with. However, given the curious mode of interaction of neutrons with atomic nuclei, we can exploit differences in the bound coherent scattering lengths of isotopes. By

<sup>i</sup> These represent the “power” of the atom / isotope at generating useful, constructive interference patterns (i.e. the actual structure factors).

doing so we change the relative weights of the individual partials contributing to the  $F(Q)$ , and give ourselves a better chance of extracting the data we need. If we allow ourselves to exchange hydrogen for deuterium, and work on the assumption that doing so does not change the system chemically or structurally, we can write a new set of weights:

$i$	$j$	$c_i$	$c_j$	$b_i, \text{fm}$	$b_j, \text{fm}$	$c_i c_j b_i b_j = w_{ij}, \text{fm}^2$
O	O	1/3	1/3	0.5804	0.5804	0.0374
O	D	1/3	2/3	0.5804	0.6674	0.0861
D	D	2/3	2/3	0.6674	0.6674	0.1980

While the weight of the O-O partial has not changed, the bound coherent scattering length of deuterium is approximately twice the magnitude of hydrogen, and is also the opposite sign, so those partials involving hydrogen are now very differently weighted in the total structure factor. The effect is clear:



We now have two independent measurements on the same system – the underlying structure in terms of the arrangement of atoms is the same, but the resulting structure factor is not. This methodology can be exploited and extended to give us structural information on materials that would otherwise not be accessible, and will be discussed in the following sections. Always keep in mind that the partial structure factors,  $S_{ij}(Q)$ , which arise from the positions of the atoms in the system, **do not vary** when changing the isotopes of the involved atoms – only the associated weighting factors change, since  $b_i$  and  $b_j$  are isotope-dependent.

## 2 Structural Correlations between Specific Atoms

We have considered a simple example so far (water), where we only have two types of atom and three resulting unique partials. Inevitably, most cases of experimental interest will contain many more atom types, and thus involve many more partials. We will often be interested in obtaining<sup>ii</sup> the structural correlations between specific groups or types of atoms within this proverbial atomic soup. From this point forward, and for the sake of clarity, we will assume that the atoms being substituted are hydrogens (for deuteriums) and employ ‘H’ and ‘D’ as the notation for ‘natural’ and ‘isotopically-substituted’ samples / atoms throughout. Of course, everything presented is still valid for other

<sup>ii</sup> It is perhaps more useful to think of this process as “highlighting” specific correlations that we deem may be important for the purposes of simulating / refining the system using EPSR, for example, to get the most relevant structural model that we can.

isotopic exchanges – e.g.  $\text{Li}^6 / \text{Li}^7$  – provided the bound coherent scattering lengths of the two isotopes differ enough to make the difference measurements feasible.

It is helpful to consider our complicated system as a very simple set containing only two atom types – H and X:

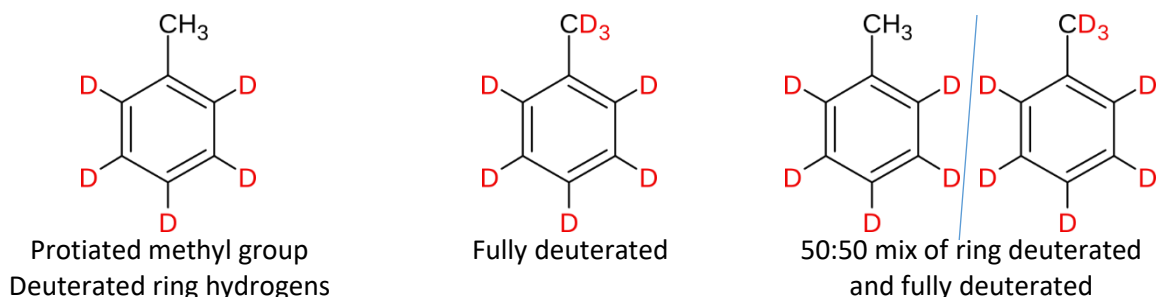
- ‘H’ represents the target atoms between which we seek to obtain the partial structure factor.
- ‘X’ is every other atom in the system.

Moreover:

- It must be possible to substitute (by some means) ‘H’ with ‘D’ in order to provide the necessary isotopic contrast.
- ‘X’ atoms, whatever element and isotope they are, remain constant in terms of element, isotope, and total atomic fraction over the HX, DX, and HDX samples.

We can then apply the measurement sets described in the following sections in order to obtain the H-H partials (as well as those between H-X and X-X).

For instance, let us say that we were interested in the correlations between methyl groups in pure toluene. Here, the ‘H’ atoms are the hydrogens of the methyl group, and the ‘X’ atoms are all the carbons and the hydrogen atoms on the benzene ring. To extract the effective partial structure factor between the methyl hydrogens, we would measure the following three samples in the ideal case (keeping all ‘uninteresting’ hydrogens as deuterium in order to reduce backgrounds):



## 2.1 Atomic Fractions of Substitution Sites

There are limits to the differences in structural signal that can reasonably be detected, so it is important to consider the atomic fractions,  $\chi$ , of the target substitution sites in the system as a whole.

For example, if you have a 1:5 mixture of ethanol:acetone:

Component	Ratio	Atoms / mol	Total Atoms	Atom%
Ethanol, $\text{C}_2\text{H}_5\text{OH}$	1	9	9	15.25
Acetone, $\text{C}_3\text{H}_6\text{O}$	5	10	50	84.75
<b>Total</b>			<b>59</b>	<b>100.00</b>
Ethanol, all H	1	6	6	10.17
Ethanol, $\text{H}_5$ only	1	5	5	8.47
Ethanol, alcohol H only	1	1	1	1.69
Acetone, all H	5	6	60	50.85

The stability of SANDALS and NIMROD is such that differences at the 1% substitution level can be detected, and for which direct subtraction of two datasets could be employed (see first-order differences in Section 2.3). For second-order differences (Section 2.4) our general recommendation is that the site of interest should make up 10 atom% of the system, with 5 atom% being the absolute minimum. So, in the ethanol:acetone example, second-order difference measurements are feasible on everything except the lone alcohol hydrogen, which makes up only 1.69 atom%.

## 2.2 Exchangeable Hydrogens

If hydrogen atoms are exchangeable – i.e. undergo fast exchange with other hydrogen atoms in the system – then care must be taken when considering substitution sites and the subsequent meaning. Primary examples of such hydrogen sites are those on alcohol (O–H) or amine (NH<sub>2</sub>) groups, although any site which is acidic enough may be subject to exchange. If all such exchangeable sites are of the same isotope (e.g. all H) then there is no cause for concern. However, if only one of several exchangeable sites is isotopically-modified, these isotopes will be smeared out over all of the exchangeable sites, and hence the effective bound coherent scattering length associated to those sites will be an average.

For instance, if we take a 50:50 mixture of ethanol:water, we know that the alcohol group on the ethanol and both hydrogens on the water are exchangeable. If we were to mix fully deuterated ethanol in a 1:1 ratio with normal, protiated water, the end result would be a system where (on average) 1/3 of all hydroxyl hydrogens would be deuterium and the remaining two thirds would be normal H. We assume that the system is well-mixed in this sense, but depending on the acidity of the exchangeable site this may not be the case in reality. For hydroxyl and amine hydrogens, exchange is rapid, and so the average picture is a good approximation given the timescales of the neutron measurements (of order 10<sup>3</sup> s).

## 2.3 First Order Differences

If we measure two isotopic samples HX and DX, we can perform a simple subtraction of one from the other in order to remove some correlations – this is a *first order difference*. Since the weighting of the X-X (composite) partial will be the same for both measurements we could simply subtract one from the other and remove the X-X contribution from the signal. Using H<sub>2</sub>O and D<sub>2</sub>O as an example:

$$\begin{aligned}
 F_{H_2O}(Q) &= 0.0374 S_{OO}(Q) - 2 \cdot 0.0482 S_{OH}(Q) + 0.0622 S_{HH}(Q) \\
 F_{D_2O}(Q) &= 0.0374 S_{OO}(Q) + 2 \cdot 0.0861 S_{OH}(Q) + 0.1980 S_{HH}(Q) \\
 F_{H_2O}(Q) - F_{D_2O}(Q) &= 0.0374 S_{OO}(Q) - 0.0374 S_{OO}(Q) \\
 &\quad - 2 \cdot 0.0482 S_{OH}(Q) - 2 \cdot 0.0861 S_{OH}(Q) \\
 &\quad + 0.0622 S_{HH}(Q) - 0.1980 S_{HH}(Q) \\
 &= -0.2686 S_{OH}(Q) - 0.1358 S_{HH}(Q)
 \end{aligned}$$

This leaves us with a signal that only contains contributions from the O-H (i.e. X-H) and H-H partials. We could of course remove / add any amount of one total structure factor from / to the other, meaning we can remove the contribution of any one partial. For instance, to remove the O-H contribution:

$$\begin{aligned}
 w_{ij}^{H_2O} &= -0.0482 \\
 w_{ij}^{D_2O} &= 0.0861
 \end{aligned}$$

$$\frac{w_{ij}^{H_2O}}{w_{ij}^{D_2O}} = \frac{-0.0482}{0.0861} = x = -0.5598$$

So:

$$\begin{aligned} F_{H_2O}(Q) - x F_{D_2O}(Q) &= 0.0374 S_{OO}(Q) - x 0.0374 S_{OO}(Q) \\ &\quad - 2 \cdot 0.0482 S_{OH}(Q) - x (2 \cdot 0.0861) S_{OH}(Q) \\ &\quad + 0.0622 S_{HH}(Q) - x 0.1980 S_{HH}(Q) \\ &= 0.0583 S_{OO}(Q) - 0.1730 S_{HH}(Q) \end{aligned}$$

Ultimately, we can do whatever algebra we wish, but with only two datasets one can never extract any pure partials.

## 2.4 Second Order Differences

We can, in fact, perform a third measurement to complement our HX and DX datasets using a mixture of the original and isotopic T components to get HDX, usually in a 50:50 ratio H:D.<sup>iii</sup> While this might not seem useful immediately, it provides us a third dataset with different weightings on the X-H and H-H partials. Taking a 50:50 mixture of H<sub>2</sub>O and D<sub>2</sub>O as an example (which gives  $c_O = c_H = c_D = 1/3$ ) the resulting partials and their weights in our new HDO sample are:

<i>i</i>	<i>j</i>	$c_i$	$c_j$	$b_i, \text{fm}$	$b_j, \text{fm}$	$c_i c_j b_i b_j = w_{ij}, \text{fm}^2$
O	O	1/3	1/3	0.5804	0.5804	0.0374
O	H	1/3	1/3	0.5804	-0.3741	-0.0241
O	D	1/3	1/3	0.5804	0.6674	0.0430
H	H	1/3	1/3	-0.3741	-0.3741	0.0155
H	D	1/3	1/3	-0.3741	0.6674	-0.0277
D	D	1/3	1/3	0.6674	0.6674	0.0495

Which gives us the following for the total structure factor:

$$\begin{aligned} F_{HDO}(Q) &= 0.0374 S_{OO}(Q) \\ &\quad + (-2 \cdot 0.0241 + 2 \cdot 0.0430) S_{OH}(Q) \\ &\quad + (0.0155 - 2 \cdot 0.0277 + 0.0495) S_{HH}(Q) \\ &= 0.0374 S_{OO}(Q) + 0.0378 S_{OH}(Q) + 0.0096 S_{HH}(Q) \end{aligned}$$

It is instructive to realise the contributions to the structure factor that we now have but, given that the timescale of the neutron measurement is long enough to allow significant atomic / molecular motion of the atoms in the system (for a liquid at any rate), we can treat the H and D as equivalent in the sense of their role in the structure, and determine the average bound coherent scattering length for a new type HD to arrive at the same result:

$$\begin{aligned} \chi_H &= 0.5, \chi_D = 1.0 - \chi_H = 0.5 \\ b_{HD} &= \chi_H b_H + (1.0 - \chi_H) b_D \\ &= 0.5 \cdot (-0.3741) + 0.5 \cdot 0.6676 \end{aligned} \tag{2}$$

<sup>iii</sup> A 50:50 ratio is usually chosen since this gives the best contrast, but it is perfectly possible to employ a higher H:D ratio if the amount of deuterated material is scarce. A 66:33 (i.e. 2:1 H:D) ratio can also provide useful contrast, but it is not recommended to use ratios higher than this.

$$= 0.1467 \text{ fm}$$

$i$	$j$	$c_i$	$c_j$	$b_i, \text{ fm}$	$b_j, \text{ fm}$	$c_i c_j b_i b_j = w_{ij}, \text{ fm}^2$
O	O	1/3	1/3	0.5804	0.5804	0.0374
O	HD	1/3	2/3	0.5804	0.1467	0.0189
HD	HD	2/3	2/3	0.1467	0.1467	0.0096

...which gives...

$$\begin{aligned} F(Q) &= 0.0374 S_{OO}(Q) + 2 \cdot 0.0189 S_{OH}(Q) + 0.0096 S_{HH}(Q) \\ &= 0.0374 S_{OO}(Q) + 0.0378 S_{OH}(Q) + 0.0096 S_{HH}(Q) \end{aligned}$$

We can now combine these three datasets in order to retrieve directly the individual correlation functions – this is a *second order difference*. If  $\chi_H$  is the fraction of H in our **mixed** (HDX) sample (as stated earlier, this is usually 0.5) then as a first step let us do a simple manipulation to remove all correlations except H-H from the signal. We write all of the weights factors explicitly for the general case:

$$\begin{aligned} \Delta F(Q) &= \chi_H F_{HX}(Q) + (1 - \chi_T) F_{DX}(Q) - F_{HDX}(Q) \\ &= \chi_H c_X^2 b_X^2 S_{XX}(Q) + 2 \chi_H c_X c_H b_X b_H S_{XH}(Q) + \chi_H c_H^2 b_H^2 S_{HH}(Q) \\ &\quad + (1 - \chi_H) c_X^2 b_X^2 S_{XX}(Q) + 2(1 - \chi_H) c_X c_D b_X b_D S_{XH}(Q) + (1 - \chi_X) c_D^2 b_D^2 S_{HH}(Q) \\ &\quad - c_X^2 b_X^2 S_{XX}(Q) - 2 c_X c_{HD} b_X b_{HD} S_{XH}(Q) - c_{HD}^2 b_{HD}^2 S_{HH}(Q) \end{aligned}$$

Rearranging by partials:

$$\begin{aligned} \Delta F(Q) &= \chi_H c_X^2 b_X^2 S_{XX}(Q) + (1 - \chi_H) c_X^2 b_X^2 S_{XX}(Q) - c_X^2 b_X^2 S_{XX}(Q) \\ &\quad + 2 \chi_H c_X c_H b_X b_H S_{OH}(Q) + 2(1 - \chi_H) c_X c_D b_X b_D S_{XH}(Q) - 2 c_X c_{HD} b_X b_{HD} S_{XH}(Q) \\ &\quad + \chi_H c_H^2 b_H^2 S_{HH}(Q) + (1 - \chi_H) c_D^2 b_D^2 S_{HH}(Q) - c_{HD}^2 b_{HD}^2 S_{HH}(Q) \\ &= 2 \chi_H c_X c_H b_X b_H S_{XH}(Q) + 2(1 - \chi_H) c_X c_D b_X b_D S_{XH}(Q) - 2 c_X c_{HD} b_X b_{HD} S_{XH}(Q) \\ &\quad + \chi_H c_H^2 b_H^2 S_{HH}(Q) + (1 - \chi_H) c_D^2 b_D^2 S_{HH}(Q) - c_{HD}^2 b_{HD}^2 S_{HH}(Q) \end{aligned}$$

We know that  $c_H = c_D = c_{HD}$  and  $c_H^2 = c_D^2 = c_{HD}^2$ , so:

$$\begin{aligned} \Delta F(Q) &= 2 c_X c_H b_X (\chi_H b_H + (1 - \chi_H) b_D - b_{HD}) S_{XH}(Q) \\ &\quad + c_H^2 (\chi_H b_H^2 + (1 - \chi_H) b_D^2 - b_{HD}^2) S_{HH}(Q) \end{aligned}$$

We earlier defined  $b_{HD} = \chi_H b_H + (1.0 - \chi_H) b_D$  (Equation 2) which zeroes the term related to  $S_{XH}(Q)$  and hence what remains is:

$$\Delta F(Q) = c_H^2 S_{HH}(Q) (\chi_H b_H^2 + (1 - \chi_H) b_D^2 - b_{HD}^2)$$

The H-H partial is thus given by:

$$S_{HH}(Q) = \frac{\chi_H F(Q)_{HX} + (1 - \chi_H) F(Q)_{DX} - F(Q)_{HDX}}{c_H^2 (\chi_H b_H^2 + (1 - \chi_H) b_D^2 - b_{HD}^2)} \quad (3)$$

Armed with this, we can now use this in our derivation of the  $S_{XH}(Q)$  partial. Let us begin by subtracting  $F_{DX}(Q)$  from  $F_{HX}(Q)$  in order to remove the X-X contribution:

$$\begin{aligned}\Delta F(Q) &= F_{HX}(Q) - F_{DX}(Q) \\ &= c_X^2 b_X^2 S_{XX}(Q) + 2c_X c_H b_X b_H S_{XH}(Q) + c_H^2 b_H^2 S_{HH}(Q) \\ &\quad - c_X^2 b_X^2 S_{XX}(Q) - 2c_X c_D b_X b_D S_{XH}(Q) - c_D^2 b_D^2 S_{HH}(Q) \\ &= (2c_X c_H b_X b_H - 2c_X c_D b_X b_D) S_{XH}(Q) + (c_H^2 b_H^2 - c_D^2 b_D^2) S_{HH}(Q)\end{aligned}$$

We are in possession of  $S_{HH}(Q)$  and so:

$$S_{XH}(Q) = \frac{F_{HX}(Q) - F_{DX}(Q) - (c_H^2 b_H^2 - c_D^2 b_D^2) S_{HH}(Q)}{(2c_X c_H b_X b_H - 2c_X c_D b_X b_D)} \quad (4)$$

For the remaining  $S_{XX}(Q)$  partial we may simply subtract our known  $S_{HH}(Q)$  and  $S_{XH}(Q)$  terms from  $F_{HX}(Q)$ :

$$\begin{aligned}F_{HX}(Q) &= c_X^2 b_X^2 S_{XX}(Q) + 2c_X c_H b_X b_H S_{XH}(Q) + c_H^2 b_H^2 S_{HH}(Q) \\ S_{XX}(Q) &= \frac{F_{HX}(Q) - 2c_X c_H b_X b_H S_{XH}(Q) - c_H^2 b_H^2 S_{HH}(Q)}{c_X^2 b_X^2}\end{aligned} \quad (5)$$

Alternatively we can subtract from the deuterated total structure factor in order to reduce the impact of noise in the resulting partial:

$$\begin{aligned}F_{DX}(Q) &= c_X^2 b_X^2 S_{XX}(Q) + 2c_X c_D b_X b_D S_{XH}(Q) + c_D^2 b_D^2 S_{HH}(Q) \\ S_{XX}(Q) &= \frac{F_{DX}(Q) - 2c_X c_D b_X b_D S_{XH}(Q) - c_D^2 b_D^2 S_{HH}(Q)}{c_X^2 b_X^2}\end{aligned} \quad (6)$$

## 2.5 Summary – Second Order Difference Equations

$$\begin{aligned}S_{HH}(Q) &= \frac{\chi_H F(Q)_{HX} + (1 - \chi_H) F(Q)_{DX} - F(Q)_{HDX}}{c_H^2 (\chi_H b_H^2 + (1 - \chi_H) b_D^2 - b_{HD}^2)} \\ S_{XH}(Q) &= \frac{F_{HX}(Q) - F_{DX}(Q) - (c_H^2 b_H^2 - c_D^2 b_D^2) S_{HH}(Q)}{(2c_X c_H b_X b_H - 2c_X c_D b_X b_D)} \\ S_{XX}(Q) &= \frac{F_{HX}(Q) - 2c_X c_H b_X b_H S_{XH}(Q) - c_H^2 b_H^2 S_{HH}(Q)}{c_X^2 b_X^2}\end{aligned}$$

## 3 Useful Substitution Sets

Here we list the sets of measurements that need to be made in order to extract certain partial correlations of interest, and assume that the substitutable atoms are hydrogens (although they can be any atoms which have suitable isotopes). There are two factors we need to consider, which limit



which sets we can measure – the number of hydrogens we are substituting, and the amount of deuterated material we have available. While the stability and background signals of the neutron instruments are good, there are limits on how subtle a difference we are able to detect. Generally speaking, we require any isotopic substitution to involve at least 5 to 10% of the total number of atoms in the system. Also, deuterated material features heavily in some of the following sets, and so the overall feasibility of the measurements will depend on the costs / effort associated with obtaining the deuterated materials.

All HD samples listed in the following tables should be made with a 50:50 mix of H:D in the ideal case, as this gives the maximum difference in scattering patterns between measurements. The ratio can be pushed a towards 2:1 H:D in order to save on the amount of deuterated material required, but at the potential cost of accuracy when manipulating the data.

### 3.1 One Site Substitution

#### 3.1.1 Ideal Case

Provided the fraction of substitutable H atoms is high enough, and if any H atoms not the focus of interest can be deuterated, the three samples listed below will yield the H-H, H-X, and X-X partials explicitly with standard counting times.

ID	Sample	Description
1	HX	Protiated target atoms with any hydrogen atoms in the remainder X substituted for deuteriums
2	DX	Fully deuterated material (all hydrogens swapped for deuteriums)
3	HDX	50:50 mixture of 1 and 2

#### 3.1.2 Less than Ideal Case

If the fraction of substitutable H atoms is high enough, but any H atoms not the focus of interest cannot be deuterated, the three samples listed below will yield the H-H, H-X, and X-X partials explicitly, but will suffer from additional noise arising from the additional hydrogen.

ID	Sample	Description
1	HX	Fully protiated material
2	DX	Hydrogens of interest substituted for deuteriums
3	HDX	50:50 mixture of 1 and 2

### 3.2 Two Site Substitution

#### 3.2.1 Ideal Case

If we have two sites 'A' and 'B' (which could be individual atoms or groups of atoms, on the same or different molecules) then the following set will yield the A-A, A-B, and B-B correlations explicitly, as well as the A-X, B-X, and of course X-X.

ID	Sample	Description
1	A <sup>H</sup> B <sup>H</sup> X	Protiated A and B sites, with any remaining hydrogens in X substituted for deuterium
2	A <sup>D</sup> B <sup>D</sup> X	Fully deuterated material
3	A <sup>HD</sup> B <sup>HD</sup> X	50:50 mixture of 1 and 2
4	A <sup>H</sup> B <sup>D</sup> X	Protiated A sites, with B sites and any hydrogens in X substituted for deuterium
5 (=2)	A <sup>D</sup> B <sup>D</sup> X	Fully deuterated material

<b>6</b>	$A^{HD}B^{DX}$	50:50 mixture of H:D for A sites, with B sites and any hydrogens in X substituted for deuterium (could be made from 50:50 mix of <b>2</b> and <b>4</b> )
<b>7</b>	$A^DB^HX$	Protiated B sites, with A sites and any hydrogens in X substituted for deuterium
<b>8 (=2)</b>	$A^DB^DX$	Fully deuterated material
<b>9</b>	$A^DB^{HD}X$	50:50 mixture of H:D for B sites, with A sites and any hydrogens in X substituted for deuterium (could be made from 50:50 mix of <b>2</b> and <b>7</b> )

This set of nine actually contains three repeats of the fully deuterated sample, so the final “magic seven” enable the full extraction of all the desired partials.

### 3.2.2 Less Than Ideal Case

If A represents the hydrogens on a solvent, and B represents those on a solute, and the solute is present in very low concentration ( $\chi_B$  will put any differences arising from isotopic substitution below the detection limit), then the only realistic option is to perform the substitution measurements on A and rely on changes in the solvent-solvent structure in order to infer the influence of the solute. In such a case B can be left in protiated form, although if it is available in deuterated form this could be used to slightly reduce incoherent background levels.

ID	Sample	Description
<b>1</b>	$A^HB^HX$	Fully protiated material
<b>2</b>	$A^DB^HX$	'A' atoms (solvent) substituted for deuteriums
<b>3</b>	$A^{HD}B^HX$	50:50 mixture of <b>1</b> and <b>2</b>

## 4 Further Reading

A good introduction to the technique of Neutron Diffraction with Isotopic Substitution is given in [“Solvent structure and perturbations in solutions of chemical and biological importance”](#), J. L. Finney, A. K. Soper, *Chem. Soc. Rev.* **23**, 1-10 (1994).

## 5 Version History

v1.0    23/11/18    First public release.