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Abstract

Isotopic substitution is used extensively in the physical sciences and particularly in vibrational spectroscopy. To be able to correctly analyze solid state spectra of crystalline materials, it is essential to know the isotopic distribution present. Here, I show how the distribution of isotopomers in a crystal may be calculated for arbitrary numbers of isotopes and sites.

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Isotopic substitution is used extensively in the physical sciences. It finds application in biochemistry *e.g.* as a tracer in studies of metabolism,[1] in neutron scattering where the different scattering lengths of hydrogen and deuterium provide contrast in small angle neutron scattering, neutron reflectometry and total scattering studies.[2] Chemistry is the area where it is probably most exploited; it is used to distinguish otherwise identical species to aid mechanistic studies but spectroscopy is the area where it is indispensable. Nuclear magnetic resonance (NMR) and Mössbauer spectroscopy are techniques that are both element and isotope specific and isotopic enrichment is often used to improve sensitivity *e.g.* ^{18}O NMR and ^{57}Fe Mössbauer. Microwave rotational spectroscopy makes use of isotopomers of the molecule of interest to improve the derived structure. The many forms of vibrational spectroscopy use isotopic substitution to aid assignment and to provide insight into coupling within and between molecules.[3,4]

While many elements are monoisotopic *e.g.* F, Na, Al, P or effectively so: ^{1}H 99.985%, ^{14}N 99.635%, ^{16}O 99.75%, there are several common elements that have significant quantities of a second isotope. These include: lithium (^{6}Li 7.5% and ^{7}Li 92.5%), boron (^{10}B 19.4% and ^{11}B 80.2%), carbon (^{12}C 98.89% and ^{13}C 1.11%), chlorine (^{35}Cl 75.77% and ^{37}Cl 24.23%) and bromine (^{79}Br 50.49% and ^{81}Br 49.31%).[5] In these cases in order to be able to analyze the spectra it is usually necessary to know how the isotopes are distributed within the molecules and this is particularly the case for vibrational spectra. The same consideration arises when a molecule is isotopically enriched.

This is trivial when there is a single site, the ratio of isotopomers is simply the natural abundance. Thus ^{13}CO$_2$ is present to the extent of 1.11% that of ^{12}CO$_2$. In the case of two isotopes, (with abundances a and b), and two sites the ratio is given by:

$$(a + b)^2 = a^2 + 2ab + b^2 \tag{1}$$

Thus for a 1:1 mixture of H_2O and D_2O, $a = b = 0.5$ and there will be 25% H_2O, 50% HOD and 25% D_2O. More generally, where there are two isotopes and n sites the distribution is given by the binomial theorem:[6]

$$(a+b)^n = \sum_{k=0}^{n} \binom{n}{k} a^k b^{n-k} \tag{2}$$

where the binomial coefficient is defined as:

$$\binom{n}{k} = \frac{n!}{k!(n-k)!} \tag{3}$$

(The coefficients in the expansion are also given by the ($n + 1$) row of Pascal's triangle). Thus for benzene with $n = 6$, the expansion is:

$$a^6 + 6a^5b + 15a^4b^2 + 20a^3b^3 + 15a^2b^4 + 6ab^5 + b^6 \tag{4}$$

For natural abundance carbon, $a = 0.989$, $b = 0.011$ and the isotopic distribution is: $^{12}C_6H_6$ 93.58%, $^{12}C_5{}^{13}CH_6$ 6.24%, $^{12}C_4{}^{13}C_2H_6$ 0.17% with $^{12}C_3{}^{13}C_3H_6$, $^{12}C_2{}^{13}C_4H_6$, $^{12}C{}^{13}C_5H_6$ and $^{13}C_6H_6$ all $<3 \times 10^{-3}$%.

Where it is only necessary to consider the isotopic distribution within a single molecule, the analysis is straightforward. The problem becomes more complex when it is necessary to consider more than two isotopes or more than one molecule. The latter situation will arise whenever there is more than one of the molecule of interest in the primitive cell of a crystalline solid. In this case it is necessary to consider the distribution of isotopomers within the material. This may be calculated using the multinomial theorem:[7]

$$\left(a+b+c+\ldots+\omega\right)^n = \sum_{k_a+k_b+k_c+\ldots+k_\omega=n}^{n} \binom{n}{k_a,k_b,k_c,\ldots k_\omega} a^{k_a} b^{k_b} c^{k_c} \ldots \omega^{k_\omega} \tag{5}$$

where the k_i are integers such that:

$$k_a + k_b + k_c + \ldots + k_\omega = n \tag{6}$$

and the multinomial coefficient is given by:

$$\binom{n}{k_a,k_b,k_c,\ldots k_\omega} = \left(\frac{n!}{k_a! k_b! k_c! \ldots k_\omega!}\right) \tag{7}$$

To illustrate the use of Eqs. (5)-(7), consider the case where the aim is to investigate the hydrogen bonding in a hydrate. Materials with more than one water molecule present commonly occur in mineralogy and gypsum, $CaSO_4.2H_2O$ is an important example of this class. There is one formula unit in the primitive cell,[8] thus there are two water molecules present. If the material is synthesised from an aqueous solution with the distribution a H_2O, b HOD and c D_2O, where $a + b + c = 1$, then from Eqs. (5) and (7):

$$\left(a+b+c\right)^2 = a^2 + b^2 + c^2 + 2ab + 2ac + 2bc \tag{8}$$

Table 1 gives the distribution for various isotopic ratios. It is often desirable to generate HOD in either a largely H_2O or D_2O environment so as to decouple the O–D (or O–H) vibration. It can be seen that to achieve this goal, a large H_2O:D_2O ratio (or *vice versa*) is the best choice.

A more complex example is when an element has two isotopes with significant abundances. This commonly occurs in boron chemistry because of the ~1:4 ratio of ^{10}B:^{11}B. Consider borazine (1,3,5,2,4,6-triazatriborinane, $B_3N_3H_6$), an inorganic analog of benzene. Assuming natural abundance, gas phase borazine will have a composition given by Eqs. (2) and (3) with $n = 3$, since there are three possible positions for the boron atoms. The resulting composition is: 0.8% $^{10}B^{10}B^{10}B$, 9.6% $^{10}B^{10}B^{11}B$, 38.4% $^{10}B^{11}B^{11}B$ and 51.2% $^{11}B^{11}B^{11}B$. For solid borazine with four molecules in the primitive cell,[9] the distribution is given by:

$$\left(a+b+c+d\right)^4 \tag{9}$$

The expansion of Eq. (9) is given in Table II. There are four useful checks that can be applied to ensure that all of the terms have been included:

Check 1: From Eq. (6), it follows that the sum of the powers must be 4 for all terms (*i.e. n* in the general case).

Check 2: The total number of terms is given by the sum of the coefficients and in general is given by m^n where m is the number of isotopomers. In this instance $m = 4$ and $n = 4$, hence there are $4^4 = 256$ terms in agreement with the last entry in column 1 of Table II.

Check 3: The number of terms involving a, b, c and d is given by:[7]

$$\begin{pmatrix} n + m - 1 \\ n \end{pmatrix} \tag{10}$$

Where the coefficient is defined in Eq. (3). For the present case, $n + m - 1 = 7$, $n = 4$ hence $7!/(4!(7-4)!) = 35$, in agreement with the last entry in column 2 of Table II.

Check 4: Eq. (5) is an *equation*, thus both sides must sum to the same value. For the special case where the sum of the isotopic abundances is unity, since $1^n = 1$, the sum of the individual compositions must also be unity (*i.e.* 100%), as seen in the last entry of column 3 of Table II. In the case where $a + b + c + ... \neq 1$ (*e.g.* if an isotope or isotopomer with low abundance is omitted) then the sum will differ from unity.

Consideration of Table II shows some surprises. As an initial guess, since ^{11}B is present to the extent of 80%, it might be expected that the crystal would be dominated by the all-^{11}B species. This is clearly not the case and it is only a minor constituent ($d^4 = 6.87\%$). The largest constituents are: $c^2d^2 = (^{10}B^{11}B^{11}B, \ ^{10}B^{11}B^{11}B, \ ^{11}B^{11}B^{11}B, \ ^{11}B^{11}B^{11}B) = 23.19\%$ and $cd^3 = (^{10}B^{11}B^{11}B, \ ^{11}B^{11}B^{11}B, \ ^{11}B^{11}B^{11}B, \ ^{11}B^{11}B^{11}B) = 20.62\%$.

The methods illustrated here are completely general and allow the isotopic distribution of a molecule or a crystal to be calculated.

TABLE I. Distribution of isotopomers of water in a crystal with a primitive cell containing two water molecules.

$H_2O:D_2O$	Molecular composition / %			Crystal composition / %					
	H_2O	HOD	D_2O	$H_2O +$ H_2O	HOD + HOD	$D_2O +$ D_2O	$H_2O +$ HOD	$H_2O +$ D_2O	$D_2O +$ HOD
9:1	81.00	9.00	1.00	65.61	3.24	0.01	29.16	1.62	0.36
3:1	56.25	37.50	6.25	31.64	14.06	0.39	42.19	7.03	4.69
1:1	25.00	50.00	25.00	6.25	25.00	6.25	25.00	12.50	25.00
1:2	11.11	44.44	44.45	1.23	19.76	19.76	9.87	9.87	39.52
1:4	4.00	32.00	64.00	0.16	10.24	40.96	2.56	5.12	40.96

TABLE II. Distribution of isotopomers of borazine in natural abundance in the primitive cell containing four molecules. ($a = {}^{10}\text{B}{}^{10}\text{B}{}^{10}\text{B} = 0.008$, $b = {}^{10}\text{B}{}^{10}\text{B}{}^{11}\text{B} = 0.096$, $c = {}^{10}\text{B}{}^{11}\text{B}{}^{11}\text{B} = 0.384$ and $d = {}^{11}\text{B}{}^{11}\text{B}{}^{11}\text{B} = 0.512$).

Coefficient	Powers	Crystal composition / %
1	a^4	0.00
1	b^4	0.01
1	c^4	2.17
1	d^4	6.87
4	a^3b	0.00
4	a^3c	0.00
4	a^3d	0.00
4	b^3c	0.14
4	b^3d	0.18
4	c^3d	11.60
6	a^2b^2	0.00
6	a^2c^2	0.01
6	a^2d^2	0.01
6	b^2c^2	0.82
6	b^2d^2	1.45
6	c^2d^2	23.19
12	a^2bc	0.00
12	a^2bd	0.00
12	a^2cd	0.02
12	b^2cd	2.17
12	ab^2c	0.03
12	ab^2d	0.05
12	ac^2d	0.72

12	bc^2d	8.70
12	abc^2	0.14
12	abd^2	0.24
12	acd^2	0.97
12	bcd^2	11.60
4	ab^2	0.00
4	ac^2	0.18
4	ad^2	0.43
4	bc^2	2.17
4	bd^2	5.15
4	cd^2	20.62
24	$abcd$	0.36
$\Sigma = 256$	Count $= 35$	$\Sigma = 100.00$

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