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The Use of a Frequency Check in the Vector Verification Method

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The frequency check, utilizing three-dimensional superpositions of the Patterson and vector verification maps, assigns relative values to positions in electron-density space which are consistent with both the Patterson function and the space group symmetry of the crystal system. These relative values — which represent the extent of peak coincidence between a Patterson and electron-density function — facilitate the choice of the first tentative atom position, a decisive factor in the success of the vector verification procedure. Employing a bivalued Patterson map, each three-dimensional superposition resulting in a relative value requires one to five seconds on a large solid state computer.

The vector verification method has been shown to be a valuable aid in the analysis of the Patterson function (Mighell & Jacobson, 1963, 1964). The procedures involved in this method are:

1. The formation of a map, referred to as a symmetry map, containing only the electron-density space positions consistent with both the Patterson function and the space group symmetry requirements of the crystal system.
2. The choice of a possible atomic position, called a tentative atom position, from the symmetry map prepared in step 1.
3. The formation of a new map, referred to as a tentative atom map, containing only the electron-density space positions consistent with the tentative atom position, in addition to the restrictions in step 1 above.
4. Repetition of steps 2 and 3 until a refinable trial model results.

The success of the vector verification method depends to a great extent upon the proper selection of the first tentative atom position. Pseudosymmetry and other factors can greatly increase the difficulty involved in this initial selection. It has been demonstrated that, in favorable cases, one correct tentative atom position may provide substantial information for the construction of trial models. Frequently, however, use of the correct tentative atom position may still retain too many points for the discernment of a refinable model. The purpose of this paper is to introduce an extension of the vector verification method to deal with these problems.

The frequency check

The frequency check method consists of a three-dimensional superposition of the Patterson function and an electron-density type function. Consider a hypothetical electron-density map which contains some extraneous peaks. Whenever the origin of the Patterson map is superimposed on an atomic position in this map, the remaining electron-density peaks in the structure will also be coincident with peaks in the Patterson map. However, if the origin of the Patterson map is not superimposed on an atomic position, the frequency of coincidences declines. Therefore, this phenomenon may be used to ascertain the true atomic locations in this electron-density map. The set of highest frequencies resulting from superpositions on each point in the electron-density map should give the most plausible atomic locations.

In reality, a symmetry map formulated by the vector verification method is used for the modified electron-density map. The Patterson map is then superimposed on each location satisfying the symmetry requirements. After each superposition, a frequency corresponding to number of peak coincidences is assigned to the superposition point, resulting in a frequency map indicative of the probable atomic locations. Once the first atomic location has been chosen, a tentative atom map is formulated by the vector verification procedure. The Patterson map may now be superimposed on each point remaining in the tentative atom map. In this case, the resultant frequencies establish a criterion for the choice of the other atomic positions.

Computational procedures

The procedures employed in this method, as illustrated by Fig. 1, are the following:

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1. A bivalued Patterson map is formulated which contains the binary digit one where the sharpened Patterson function is greater than an arbitrary threshold value and the binary digit zero where below; these digits are stored in consecutive binary positions of memory. Thus, in practically all cases, a line requires at most two memory locations for storage. Each P in Fig. 1(a) designates a Patterson map position having a value above the threshold.
2. Utilizing the bit representation of the Patterson map, a symmetry map is calculated by the vector verification procedure. Fig. 1(b) illustrates such a map, where each S denotes a position in electron-density space consistent with the Patterson function and the space group requirements of the crystal system.
3. Fig. 1(c) illustrates a three-dimensional superposition of the Patterson and symmetry maps. The frequency of coincidences assigned to the superposition point in Fig. 1(c) would be twelve; each F denotes the coincidence of a P and S. For the case shown in Fig. 1, the Patterson map would be superimposed on each S point in the symmetry map, a total of eighteen superpositions. After each superposition, the frequency of coincidences is assigned to the superposition point.

In the computer, the maps are compared one line at a time, using a logical 'AND' procedure. The number of ones remaining is then added to the frequency. On the Control Data Corporation 1604 computer, the full three-dimensional comparison is performed in one to five seconds, depending upon the map size and the number of binary ones present.

Experimental results

To investigate the utility of the frequency check, calculations were performed on two compounds whose structures had already been determined by other methods. The first structure, B_8Cl_8 (Jacobson & Lipscomb, 1958), crystallizes in the space group $P2_12_12_1$ which has four equivalent positions. As an illustration of the difficulty involved in the selection of a tentative atom position, consider the symmetry map for B_8Cl_8 given in Fig. 2. Each S represents an electron-density space location consistent with the B_8Cl_8 Patterson map and the symmetry of the space group. Consequently, S appears only at those positions (x, y, and z) where the vectors $(\frac{1}{2}-2x, -2y, \frac{1}{2})$, $(\frac{1}{2}, \frac{1}{2}-2y, -2z)$, and $(-2x, \frac{1}{2}, \frac{1}{2}-2z)$ are present in the Patterson map ($80\times40\times80$). There are two chlorine atoms in section 2/80 of the B_8Cl_8 electron-density map. The darkened S positions in Fig. 2 denote these atomic locations. Any darkened S position could be chosen as the first tentative atom position.

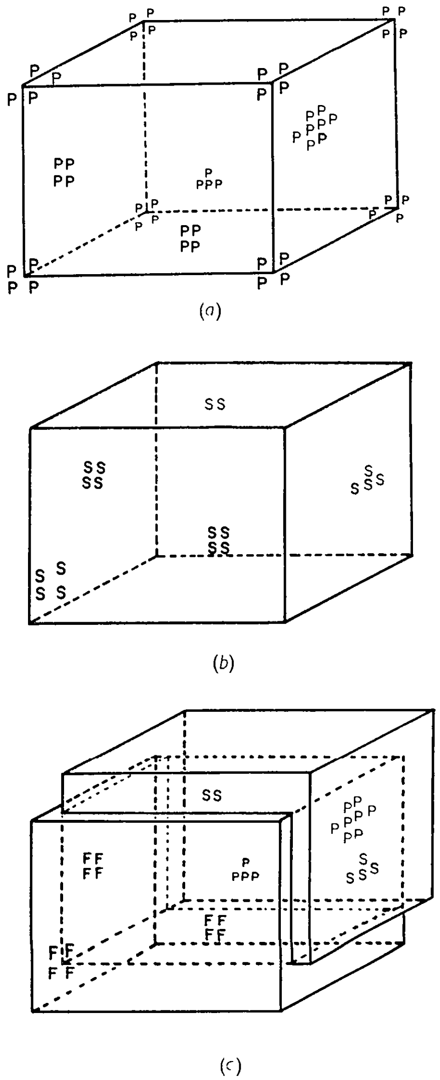


Fig. 1. (a) and (b) represent bivalued Patterson and symmetry maps respectively. (c) A typical three-dimensional superposition of the bivalued Patterson and symmetry maps.

The frequency map in Fig. 3 is the result of applying the frequency check method to the symmetry map in Fig. 2. In this frequency map, the two clusters of highest frequency represent the two chlorine atoms. The position having the highest frequency was then used as the first tentative atom position in the vector verification method. When the frequency check method is applied to this tentative atom map, the resultant frequencies indicate the other chlorine position. These frequencies are given in Fig. 4.

The second known structure, the photodimer of 2-amino-5-chloro-pyridine hydrochloride ($C_{10}H_{10}N_4Cl_2$. 2HCl.2H_2O) crystallizes in the triclinic crystal system, space group $P1$, with one dimer molecule per unit cell. The structure was originally determined (Gorres & Jacobson, 1964) by the heavy atom method in con-

Fig. 2. This section of the B_8Cl_8 symmetry map was calculated with a threshold value of 100 in the Patterson map. Darkened positions indicate the choices for the first tentative atom position which would be consistent with the refined chlorine positions.

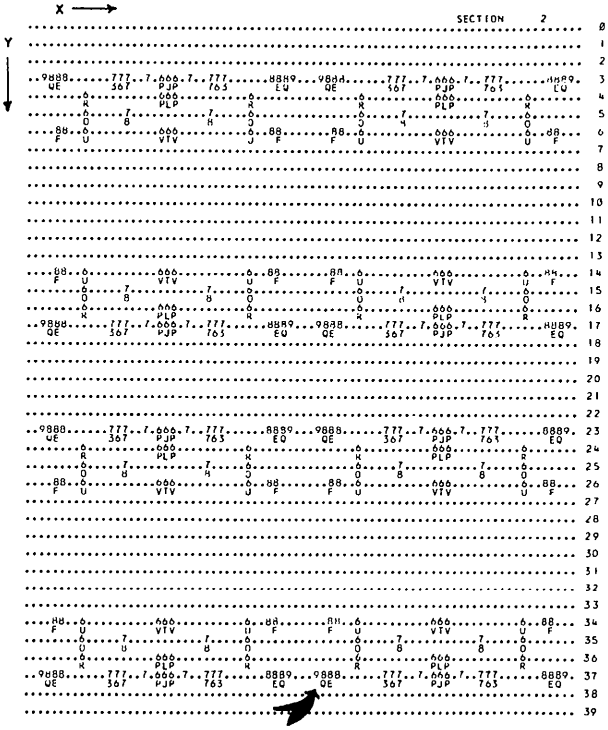


Fig. 3. This frequency map displays the frequencies of the B_8Cl_8 symmetry map given in Fig. 2. The highest frequency is designated by an arrow. The output code consists of two characters per grid point. The numbering sequence is modular 32, *i.e.* 0, 1, . . . , 9, *A*, *B*, . . . , *U* represents 0 through 31. To convert the code to its numerical value, multiply the top character's value (same level as periods) by 32 and add the lower character's value.

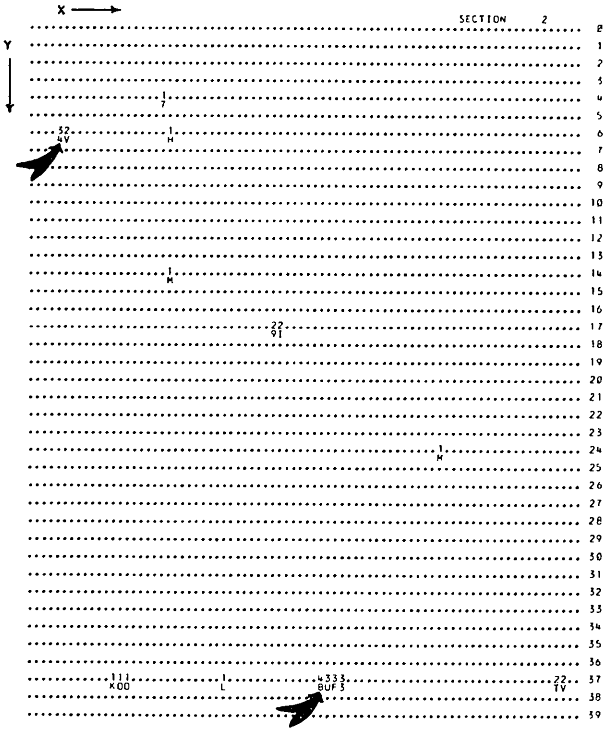


Fig. 4. This frequency map displays the frequencies of the B_8Cl_8 tentative atom map using the chlorine position (42, 37, 2) indicated in Fig. 3 as the first tentative atom position. The refined positions were (4, 6, 2) and (42, 37, 1). The observed positions are (4, 6, 2) and (42, 37, 2), respectively. These two chlorine positions are indicated by arrows.

junction with superpositions employing the Buerger minimum function. Fig. 5 illustrates the dimer molecule but does not show the chloride or oxygen atoms present in the unit cell. Because of the relative ease in finding the chlorine and chloride atom positions originally, the frequency check analysis was initiated on a tentative atom map employing the refined coordinates of these two atoms. The photodimer's

Table 1. *The frequencies of the 2-amino-5-chloropyridine hydrochloride photodimer tentative atom maps*

These maps were calculated with a threshold of forty in the Patterson map. Excess peaks have been included only if their frequencies are equal to or greater than those of the correct positions listed. Coordinates in bold type refer to the positions used in the calculation of the tentative atom map prior to the application of the frequency check method

	Calc.			Observed				Observed			
Atom	*x*	*y*	*z*	*x*	*y*	*z*	Freq.	*x*	*y*	*z*	Freq.
Cl	41	11	2	**41**	**11**	**2**	4468	**41**	**11**	**2**	2333
Cl^-	29	14	16	**29**	**13**	**16**	4468	**19**	**13**	**16**	2333
O	20	26	7	19	25	7	3120	**19**	**25**	**7**	2333
C(4)	5	4	11	4	4	11	3080	4	2	12	1820
C(2)	45	38	13	45	37	13	3048	45	38	13	1740
N(2)	46	31	13	46	31	14	2920	46	31	14	1670
C(3)	7	46	17	6	46	14	2872	9	43	16	1590
N(1)	37	38	10	37	39	10	2864	37	38	9	1590
C(5)	44	4	9	44	4	8	2888	44	4	8	1600
C(6)	38	46	12	not present							
	Extra			26	38	6	2960	—	—	—	—
	Extra			0	24	0	2864	—	—	—	—
	Extra			12	30	3	2872	—	—	—	—
	Extra			—	—	—	—	12	10	9	1590
	Extra			—	—	—	—	37	27	16	1590

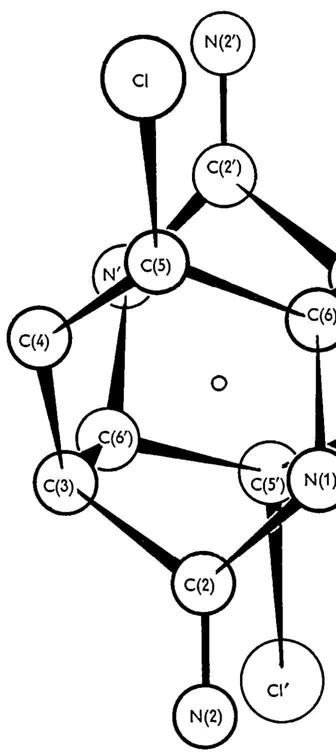


Fig. 5. The 2-amino-5-chloropyridine hydrochloride photodimer.

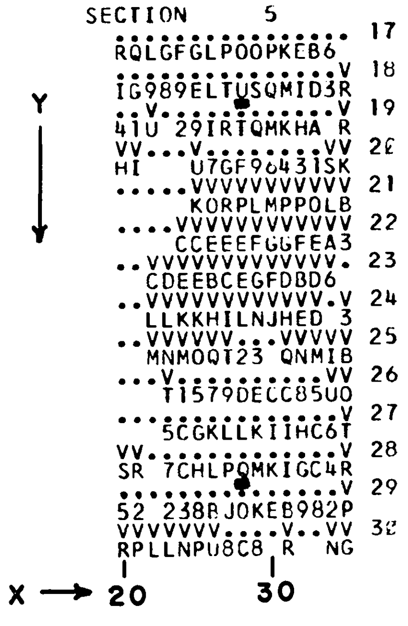
Patterson map is calculated with intervals of 48 × 48 × 40 (approximately 0·17 Å) along **a**, **b**, and **c**, respectively. Table 1 gives a comparison of the refined and observed atomic positions (*via* the highest frequency) in terms of the interval along **a**, **b**, and **c** (x, y, and z). The chlorine and chloride atoms gave the two highest frequencies; the next highest frequency corresponded to the position of the oxygen atom. Using these three atomic positions, a second tentative atom map was then calculated. The frequencies of this map indicated the correct positions for six of the remaining seven atoms. In general, care must be exercised in the choice of the threshold value since too large a threshold value may cause elimination of the correct positions as probably occurred with the last carbon of Table 1.

Use of the frequency check on structures containing heavy atoms would normally follow the sequence displayed in Table 1. To ascertain the method's value in finding atomic locations without assuming tentative atom positions, the frequencies of the 2-amino-5-chloropyridine hydrochloride photodimer's symmetry map were calculated. These frequencies are given in Table 2; nine of the ten atoms are found in the highest frequencies of the symmetry map, using a threshold of 75. Three other points have frequencies between 420 and 450. Since the chlorine and chloride peaks are the highest frequencies, these atomic positions could then be used to calculate tentative atom maps as previously described.

Table 2. *The frequencies of the* 2-*amino*-5-*chloropyridine hydrochloride photodimer symmetry map, calculated with a threshold value of* 75

	Calc.			Observed			
Atom	x	y	z	x	y	z	Freq.
Cl	41	11	2	40	10	2	510
Cl^-	29	14	16	31	13	17	510
O	20	26	7	19	27	7	480
C(4)	5	4	11	4	2	11	420
C(2)	45	38	13	45	37	14	480
N(2)	46	31	13	46	34	15	450
C(3)	7	46	17	——not present——			
N(1)	37	38	10	38	37	10	480
C(5)	44	4	9	43	3	8	450
C(6)	38	46	12	38	47	16	460

In the B_8Cl_8 case, the eight chlorine atoms provide enough information to establish the entire structure. Of interest, however, is the application of the frequency check method to this structure in an attempt to locate the boron atom positions. Since the method of comparing bits does not retain the peak value, there is no direct correlation between the magnitude of the frequencies and the atomic number. On the other hand, the relative frequencies obtained are a function of



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SECTION     5
................ 17
RQLGFGLPOOPKEB6
...............V 18
IG989ELTUSQMID3R
..V............V 19
41U 29IRTQMKHA R
VV...V........VV 20
HI   U7GF96431SK
.....VVVVVVVVVVV 21
     KORPLMPPOLB
....VVVVVVVVVVVV 22
    CCEEEFGGFEA3
..VVVVVVVVVVVVV. 23
  CDEEBCEGFDBD6
..VVVVVVVVVVVV.V 24
  LLKKHILNJHED 3
..VVVVVV...VVVVV 25
  MNMOQT23 QNMIB
...V..........VV 26
   TI579DECC85UO
...............V 27
   5CGKLLKIIHC6T
VV.............V 28
SR 7CHLPQMKIGC4R
...............V 29
52 238RJOKEB982P
VVVVVVV....V..VV 30
RPLLNPU8C8 R  NG
```

Fig. 6. A frequency map indicating the location of two boron atoms in the B_8Cl_8 crystal structure. The highest frequency in each cluster is underlined. The refined positions were (26, 28, 5) and (28, 19, 5). The observed positions are (28, 28, 5) and (28, 18, 5), respectively. A constant is subtracted from each frequency for the output routine. A negative number is represented by a V on the top line in the output code previously described.

the threshold employed. The difficulties involved in locating the boron atoms are primarily caused by improper selection of the low threshold value (Gorres & Jacobson, 1963). However, if no symmetry map is calculated — that is, a tentative atom map is calculated as the first step — then a high threshold may be employed since only peaks corresponding to boron–chlorine vectors need be found in the Patterson map to locate the boron positions. This approach was utilized in the calculation of the frequency map in Fig. 6.

Extension of the frequency check

The vector verification method employs the space group symmetry requirements in the formulation of symmetry and tentative atom maps. By taking into account the three-dimensional peak coincidences of the Patterson and electron-density functions, the frequency check provides more evidence in discerning atomic positions. In these procedures, valuable information — the actual value of the Patterson function — is unused. A value from the Patterson map could be applied to each point in the symmetry map, *i.e.* the lowest value encountered in checking the vectors in the Patterson map. During the frequency check, instead of summing the number of bit coincidences, the minimum value could be summed where two values coincide. In this manner, the value assigned to each electron-density position would take into consideration the space group symmetry requirements, the values of the Patterson function, and the three-dimensional aspect of the Patterson and electron-density peak coincidences. Of course, compared with the bivalued Patterson procedure, this approach would require a significant increase in both the computational time and the machine storage requirements.

Although the symmetry and tentative atom maps have been substituted for the hypothetical electron-density map in our discussion, the frequency check is not restricted to such comparisons. There are advantages in applying the frequency check procedure to superposition maps formulated in the usual manner. For instance, the frequencies resulting from superimposing the original Patterson map on the remaining points in the superposition map — that is, the map resulting from a superposition using the Buerger minimum function — should facilitate the discernment of coincidence peaks from true peaks.

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