

Karle–Hauptman Matrices and Eigenvalues: a Practical Approach

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(Received 14 April 1997; accepted 14 October 1997)

Abstract

The possible usefulness of eigenvectors and eigenvalues of Karle–Hauptman matrices is examined. The eigenvalue spectra of structures with calculated and measured $|U|$'s are discussed and the result of several attempts at phase refinement are reported. The use of the sum of the square of the negative eigenvalues (SSNE) as a goodness-of-fit criterion is examined. The possible use of *a priori* information is investigated using the approximation of orthogonal electron densities corresponding to eigenvectors with eigenvalues greater than zero.

1. Introduction

The nomenclature used in this paper is given in Table 1.

In an earlier paper (van der Plas *et al.*, 1998), the algebraic properties of large Karle–Hauptman matrices were examined and the information obtainable from the eigenvalues and eigenvectors of these matrices was investigated. It was found that for calculated reflections the eigenvalue spectrum of a Karle–Hauptman matrix contains a maximum of N eigenvalues with values greater than zero and (if $n > N$) $n - N$ eigenvalues exactly equal to zero. This result leads directly to the assumption that the properties of eigenvalues and eigenvectors might be used in an algebraic approach to the phase problem, as an alternative to the probabilistic approach commonly associated with direct methods.

Since in practice Karle–Hauptman matrices filled with random phases generally contain negative eigenvalues, algorithms were developed to minimize the SSNE. Two possibilities are reported in this paper: one uses the eigenvectors with positive eigenvalues to construct a new matrix, the second consists of squaring the Karle–Hauptman matrix. Both algorithms are based on the properties of Karle–Hauptman matrices with correct phases: a Karle–Hauptman matrix with correct phases can be reconstructed using only the eigenvectors corresponding to positive eigenvalues (although this is an approximation when measured reflections are used) and a Karle–Hauptman matrix with correct phases equals its own square (again an approximation when finite matrices are used). These properties were derived in the previous paper.

Table 1. Nomenclature

| | |
|---------------------------|---|
| N | Number of atoms in the unit cell |
| n | Order of a matrix |
| λ_j, \mathbf{e}_j | The j th eigenvalue and corresponding eigenvector |
| \mathbf{h} | Index array for generating Karle–Hauptman matrices: $A_{ij} = E^{\mathbf{h}(j) - \mathbf{h}(i)}$ |
| SSNE | Squared sum of negative eigenvalues |

Table 2. Eigenvalues as a function of the dimension

| Eigenvalue | Dimension 5 | Dimension 10 | Dimension 500 |
|------------|-------------|--------------|---------------|
| 1 | 0.2770 | 1.2992 | 99.5125 |
| 2 | 0.8320 | 1.6208 | 99.5940 |
| 3 | 1.1407 | 2.1128 | 99.6575 |
| 4 | 1.3220 | 2.3101 | 100.463 |
| 5 | 1.4283 | 2.6567 | 100.772 |

Table 3. Experimental data

| | |
|----------------------|-------------------|
| Compound | RN001 |
| Composition | $C_{21}O_3H_{28}$ |
| Space group | $P2_1$ |
| No. of units in cell | 2 |

2. Eigenvalue spectra

First, the behaviour of the eigenvalues of Karle–Hauptman matrices corresponding to a small structure (structure I) is examined. The test structure was one-dimensional, consisting of five atoms at random positions along the a axis. Several Karle–Hauptman matrices of varying orders were constructed. For each matrix, the eigenvalues were obtained using calculated $U(\mathbf{H})$'s. The number of non-zero eigenvalues for each matrix was independent of the order of the matrix and equal to the number of atoms in the cell (five). Since U 's were used in the Karle–Hauptman matrices, the average non-zero eigenvalue now has a value of n/N and not 1, which is the average when the reflections as defined by Main (1975) are used. The values of the non-zero eigenvalues are given in Table 2. Clearly, as the matrices become larger, the difference between the non-zero eigenvalues becomes smaller. This is in agreement with theory.

Finally, we examined the eigenvalue spectrum of RN001, a small steroid structure (see Table 3). The calculations were performed with $|U|$'s based on

Table 4. Eigenvalues of RN001 (75 × 75 matrix)

| Phase set | SSNE | Lowest negative eigenvalue | No. of negative eigenvalues | Average phase error (°) |
|--------------------------------|--------|----------------------------|-----------------------------|-------------------------|
| Correct phase set, not refined | 1.295 | -0.65 | 16 | 1 |
| Correct phase set, refined | 0.907 | -0.44 | 21 | 11 |
| Random phase set, not refined | 30.287 | -2.57 | 22 | 80 |
| Random phase set, refined | 8.737 | -1.08 | 27 | 73 |

measured intensities. In Fig. 1, the lowest eigenvalues of a Karle-Hauptman matrix of dimension 75 filled with two different phase sets are displayed: one phase set corresponding to the structure and a random phase set. Both sets have been refined using an algorithm that is given in the refinement section. Clearly, the Karle-Hauptman matrix has negative eigenvalues regardless of the quality of the phase set, indicating that the strict non-negativity no longer holds for unitary structure factors based on measured intensities. This can be contributed to errors in the scaling of the $|U|$'s and the errors in the measurement. If semipositivity can no longer be used, a new criterion to investigate the quality of a phase set is needed. The sum of the squares of the negative eigenvalues (SSNE) is a natural choice for such a criterion. Applying this criterion to the phase sets in Fig. 1 gives the results shown in Table 4. Other criteria are also shown: the first column gives the SSNE, the second column gives the smallest eigenvalue, the third one reports the number of negative eigenvalues and the final column gives the average phase error of the phase sets, calculated over the 276 strong reflections present in the matrix.

These values indicate that even though the Karle-Hauptman matrix is no longer semipositively definite for larger orders, using U values based on measured intensities, the number and value of the negative eigenvalues still give a clear indication of the relation between the structure and the phase sets.

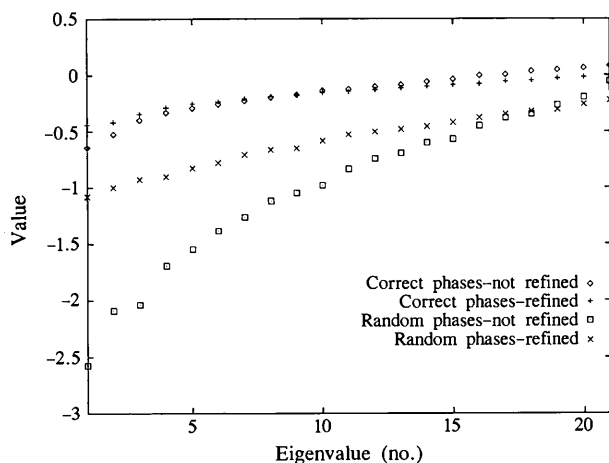


Fig. 1. Lowest eigenvalues of RN001.

3. Eigendensities

After the calculation of the eigenvalues and eigenvectors, it is possible to calculate the contribution of each eigenvector to the electron density obtainable from the Fourier transform of the reflections in the Karle-Hauptman matrix. The density corresponding to one eigenvector is called an eigendensity, after the terminology used by Main (1975).

The contribution of the i th eigenvector to the electron density can be calculated by generating the matrix

$$\mathbf{KH}'_i = \mathbf{e}_i \lambda_i \mathbf{e}_i^* \quad (1)$$

and using the elements in the matrix \mathbf{KH}'_i as structure factors for a Fourier transformation. Because the sum over all \mathbf{KH}'_i is equal to the original Karle-Hauptman matrix, the sum of these eigendensities is equal to the electron density obtained by taking all the structure factors in the Karle-Hauptman matrix and using them in a Fourier transformation. The exact formula used for the calculation of electron density is formula (30) in the preceding paper:

$$\rho(\mathbf{x}) = \sum_{k=1, l=1, k \neq l}^n \lambda_j (e_{jk} \bar{e}_{jl} + \varepsilon_j) \times \exp\{-2\pi i[\mathbf{h}(l) - \mathbf{h}(k)] \cdot \mathbf{x}\}, \quad (2)$$

in which ε_j is the average value of the diagonal elements in the matrix $\mathbf{B}_j = \mathbf{e}_j \lambda_j \mathbf{e}_j^*$, namely $\langle e_{jk} \bar{e}_{jk} \rangle_k$. For more information and the difference between this approach and the original approach used by Main, we refer to the preceding paper.

Using calculated unitary structure factors, it is expected that the sum of the eigendensities is exactly the structure, the only possible difference being caused by the absence of reflections not present in the Karle-Hauptman matrix used in the calculations. To investigate the properties of these eigendensities, the one-dimensional structure used in the previous paragraph is examined. A sample of the results of the calculation of the eigendensities corresponding to two eigenvectors of a 20×20 Karle-Hauptman matrix is shown in Figs. 2 and 3. The eigendensities were calculated from two different Karle-Hauptman matrices, one with a simple indexing array, namely $\mathbf{h} = 1, 2, 3, 4, 5, \dots$, resulting in a large redundancy of reflections in the Karle-Hauptman matrices (Fig. 2) and the second one with an array $\mathbf{h} = 1, 2, 4, 7, 11, \dots$, resulting in minimum

redundancy (Fig. 3). Matrices with a large redundancy contain a large number of identical reflections. For example, with the simple indexing array, the reflection U_1 occurs $n - 1$ times. The Karle–Hauptman matrices are generated by the indexing array as follows: an element at position (i, j) is given by $U_{\mathbf{h}(j) - \mathbf{h}(i)}$. The sum of the eigendensities of the five eigenvectors with non-zero eigenvalues equals the original structure in both cases, although there is a difference in the sharpness of the peaks. This is also in accordance with theory.

In Fig. 2, the simple indexing array results in contributions from many low-order reflections (the highest order is $20 - 1 = 19$). Thus, the peaks are not as sharp as in Fig. 3. In both figures, clearly the electron density of the eigendensities is not distributed evenly among the peaks. This does not follow directly from the definition but it was shown in the preceding paper that for large matrices the eigendensities are approximately orthogonal. This implies that, if the electron density at

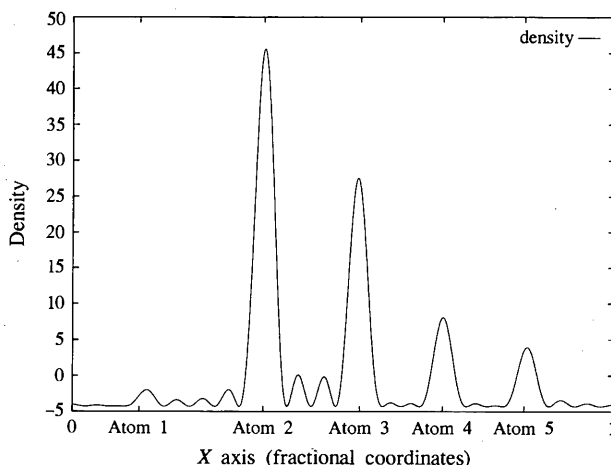


Fig. 2. Eigendensity corresponding to \mathbf{e}_1 , large redundancy.

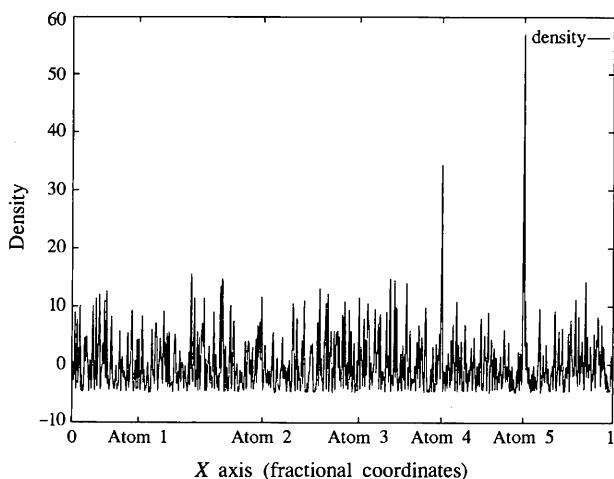


Fig. 3. Eigendensity corresponding to \mathbf{e}_2 , small redundancy.

nonpeak positions is zero, the electron-density distribution over the peaks cannot be even. It seems likely that for smaller matrices the electron-density distribution is also uneven.

The uneven distribution of density over the eigendensities is of possible use in phase refinement. In the next section, methods will be discussed for phase refinement in which eigendensities play an important part. When a small part of the structure is known, one can regard this part as if it was a contribution from an eigendensity and thus use it to generate a new phase set, partly based on the known part of the structure. This will be discussed further in the next section.

4. Phase refinement

Several techniques to optimize the eigenvalue spectrum as a function of the phases were tried. By optimization is meant trying to minimize the SSNE. As was explained in the preceding paper and the earlier sections of this paper, this is a suitable criterion for phase sets in Karle–Hauptman matrices, provided there is redundant symmetry in the matrix (de Gelder, Elout, de Graaff & Schenk, 1993). Main (1975) also proposed several refining routines based on eigenvalues and eigenvectors.

Owing to the complexity of the problem, simple linear optimization routines such as *Simplex* are insufficient. Routines were designed based on several specific properties of large Karle–Hauptman matrices. The first routine is based on the fact that any semi-positive Karle–Hauptman matrix can be written as the sum of its positive eigenvalues and -vectors by

$$\mathbf{KH} = \sum_{i=1}^N \mathbf{e}_i \lambda_i \mathbf{e}_i^*, \quad (3)$$

where \mathbf{e}_i is the eigenvector corresponding to the eigenvalue λ_i , which is greater than zero (van der Plas *et al.*, 1998). Note that this only holds exactly when calculated $|U|$'s are used, but the approximation is acceptable when the orders are about $2N$ or larger. That the deviation from the theoretical eigenvalue spectrum, resulting from the use of measured $|U|$'s, is not too large may be seen in the eigenvalue spectrum of RN001, as discussed in the previous paragraph.

The refinement method consists of generating a Karle–Hauptman matrix containing the measured $|U|$ values and random phases. Next, the eigenvalues and -vectors are calculated and a new Karle–Hauptman matrix is generated by taking the positive eigenvalues and the corresponding eigenvectors and substituting them in (3). From this new matrix, only the phases are substituted in the original matrix and the process is repeated until convergence or a maximum number of cycles is reached.

Table 5. Results of method one: generating a new Karle-Hauptman matrix from the eigenvectors corresponding to positive eigenvalues

The number of cycles indicates how many times this method was applied. The results for each number of cycles are given in three columns. The first column gives the average error in the phase set, the second the SSNE and the third column indicates whether *AUTOFOUR* was able to solve the structure with the phase set produced.

| Phase set | | 0 cycles | | | 50 cycles | | | 500 cycles | | | 2000 cycles | | |
|-----------|--------------|----------|--------|-----|-----------|-------|-----|------------|-------|-----|-------------|-------|-----|
| 1 | (51 by 51) | 80 | 13.58 | No | 76 | 5.23 | Yes | 74 | 1.40 | No | 56 | 0.61 | Yes |
| | (101 by 101) | 79 | 54.04 | Yes | 75 | 24.93 | No | 72 | 12.80 | No | 69 | 7.63 | Yes |
| | (151 by 151) | 81 | 132.27 | No | 79 | 75.44 | No | 66 | 29.67 | Yes | 55 | 17.69 | Yes |
| 2 | (51 by 51) | 79 | 12.95 | No | 75 | 3.60 | No | 71 | 1.32 | Yes | 54 | 0.69 | Yes |
| | (101 by 101) | 81 | 59.58 | No | 76 | 23.64 | No | 66 | 10.50 | Yes | 50 | 6.21 | Yes |
| | (151 by 151) | 80 | 129.33 | No | 76 | 70.33 | Yes | 74 | 29.96 | No | 64 | 16.73 | No |
| 3 | (51 by 51) | 78 | 14.47 | No | 74 | 3.68 | No | 73 | 1.42 | No | 67 | 1.11 | Yes |
| | (101 by 101) | 79 | 61.20 | Yes | 76 | 27.50 | No | 78 | 9.31 | No | 79 | 7.23 | No |
| | (151 by 151) | 81 | 119.13 | Yes | 80 | 72.06 | Yes | 77 | 35.36 | No | 60 | 21.00 | Yes |
| 4 | (51 by 51) | 79 | 13.53 | Yes | 70 | 3.93 | No | 77 | 1.03 | Yes | 75 | 0.59 | No |
| | (101 by 101) | 79 | 58.64 | No | 79 | 24.97 | Yes | 77 | 10.02 | No | 78 | 7.04 | No |
| | (151 by 151) | 83 | 125.70 | Yes | 79 | 73.19 | Yes | 76 | 35.33 | Yes | 77 | 23.87 | No |
| 5 | (51 by 51) | 77 | 17.42 | No | 80 | 4.33 | No | 76 | 1.02 | No | 66 | 0.54 | Yes |
| | (101 by 101) | 81 | 58.77 | No | 81 | 27.54 | No | 73 | 11.96 | Yes | 73 | 8.59 | Yes |
| | (151 by 151) | 80 | 126.96 | No | 77 | 74.27 | Yes | 75 | 33.07 | Yes | 68 | 19.59 | No |
| 6 | (51 by 51) | 78 | 10.82 | No | 74 | 3.42 | No | 73 | 1.38 | Yes | 68 | 1.06 | No |
| | (101 by 101) | 80 | 57.83 | No | 79 | 26.97 | No | 76 | 13.29 | Yes | 52 | 7.97 | No |
| | (151 by 151) | 84 | 123.61 | No | 81 | 70.18 | Yes | 76 | 26.50 | No | 77 | 15.96 | No |
| 7 | (51 by 51) | 79 | 13.83 | No | 76 | 5.06 | No | 71 | 1.20 | No | 76 | 0.83 | No |
| | (101 by 101) | 80 | 59.24 | Yes | 77 | 27.41 | Yes | 63 | 9.14 | Yes | 37 | 4.08 | Yes |
| | (151 by 151) | 82 | 124.99 | Yes | 81 | 69.74 | No | 74 | 29.90 | No | 71 | 26.46 | No |
| 8 | (51 by 51) | 76 | 14.39 | No | 75 | 4.05 | No | 74 | 1.38 | No | 76 | 1.32 | Yes |
| | (101 by 101) | 83 | 51.46 | No | 83 | 23.31 | No | 82 | 10.47 | No | 75 | 7.23 | No |
| | (151 by 151) | 82 | 123.96 | Yes | 81 | 67.88 | Yes | 80 | 31.78 | No | 67 | 13.42 | No |
| 9 | (51 by 51) | 77 | 13.13 | Yes | 70 | 3.11 | Yes | 64 | 0.87 | Yes | 64 | 0.71 | Yes |
| | (101 by 101) | 81 | 49.00 | Yes | 79 | 23.42 | No | 71 | 8.78 | Yes | 52 | 5.81 | No |
| | (151 by 151) | 80 | 136.77 | Yes | 80 | 78.36 | No | 79 | 37.70 | No | 78 | 25.76 | No |
| 10 | (51 by 51) | 80 | 12.85 | No | 79 | 4.80 | No | 75 | 1.54 | No | 76 | 1.01 | No |
| | (101 by 101) | 81 | 53.42 | No | 81 | 25.12 | No | 78 | 11.71 | No | 80 | 8.24 | No |
| | (151 by 151) | 81 | 118.41 | No | 80 | 67.51 | Yes | 71 | 27.32 | Yes | 70 | 21.28 | No |

The second routine is based on the fact that in the infinite case, for equal atoms and when the phases are correct, a Karle-Hauptman matrix equals its own square. Again, random phases are assigned to the $|U|$'s in the matrix but now the matrix is squared and the phases in the new matrix are substituted in the original matrix and the process is repeated until convergence or the maximum number of cycles is reached. Note that this procedure is equivalent to applying the Sayre equation to the reflection KH_{ij} using the elements in the i th row and the j th column.

The matrices were generated according to the procedures described by de Gelder, de Graaff & Schenk (1993). In order to regulate the refinement, fudge factors were applied to mediate the new and the old phase sets. These fudge factors represent the weight of the new phase set, ranging from 1 to 0. In the first refinement routine, the fudge factors were based on the squared sum of the negative eigenvalues (SSNE): if the SSNE decreases, the fudge factor is increased and *vice versa*. In the second routine, the fudge factors are inversely proportional to the difference in $|U|$ between the original entry in the matrix and the corresponding entry in the squared matrix. It was found that 'fudging'

was especially important using matrix squaring, since this represents a Sayre approximation over only a limited number of terms.

The refinement methods described above were used both separately and in combination, the results are shown in Tables 5, 6 and 7. In all experiments, ten random phase sets were generated and refined. The resulting phase sets were compared with the correct phase set to find a phase error and a Fourier transform was performed to find peak positions corresponding to the phase sets. The atomic positions were used as input for the program *AUTOFOUR* (Kinneging & de Graaff, 1984), a Fourier recycling program that tries to extend the starting positions into the complete crystal structure.

The tables contain the following information: In the first column, the phase set and the dimension of the matrix are given. In the next column, the average error in the phase set is given, followed by the SSNE. (In Table 6, where this figure is unavailable, the entry is an indication of how close the magnitude of the calculated reflections is to the measured reflections.) The next entry indicates whether or not the structure was solved by the *AUTOFOUR* program. This is repeated in the

Table 6. Results of method two: generating a new Karle–Hauptman matrix by squaring the original matrix

The number of cycles indicates how many times this method was applied. The results for each number of cycles are given in three columns. The first column gives the average error in the phase set, the second gives an indication of the difference between the old and new matrices, and the third column indicates whether *AUTOFOUR* was able to solve the structure with the phase set produced.

| Phase set | 0 cycles | | | 50 cycles | | | 500 cycles | | | 2000 cycles | | |
|-----------|--------------|----|-------|-----------|-------|-----|------------|-------|-----|-------------|-------|-----|
| 1 | (51 by 51) | 79 | – No | 49 | 1817 | Yes | 43 | 2162 | Yes | 43 | 2169 | Yes |
| | (101 by 101) | 79 | – Yes | 61 | 7756 | No | 38 | 9311 | Yes | 38 | 9331 | Yes |
| | (151 by 151) | 81 | – No | 47 | 25145 | Yes | 42 | 25868 | Yes | 45 | 25790 | Yes |
| 2 | (51 by 51) | 79 | – No | 46 | 1607 | Yes | 43 | 2168 | Yes | 43 | 2175 | Yes |
| | (101 by 101) | 81 | – Yes | 50 | 8396 | Yes | 72 | 9701 | No | 73 | 9796 | Yes |
| | (151 by 151) | 80 | – No | 44 | 24513 | Yes | 39 | 25893 | Yes | 41 | 25818 | Yes |
| 3 | (51 by 51) | 78 | – Yes | 48 | 1767 | Yes | 43 | 2175 | Yes | 43 | 2175 | Yes |
| | (101 by 101) | 79 | – Yes | 63 | 7992 | No | 41 | 9322 | Yes | 40 | 9343 | Yes |
| | (151 by 151) | 81 | – Yes | 46 | 21974 | Yes | 49 | 23076 | No | 44 | 25734 | Yes |
| 4 | (51 by 51) | 79 | – No | 67 | 2099 | No | 65 | 2175 | No | 65 | 2181 | No |
| | (101 by 101) | 79 | – No | 79 | 8046 | No | 72 | 9767 | No | 72 | 9779 | No |
| | (151 by 151) | 83 | – Yes | 58 | 20571 | Yes | 48 | 25473 | Yes | 47 | 25640 | Yes |
| 5 | (51 by 51) | 77 | – Yes | 67 | 2090 | No | 66 | 2143 | No | 65 | 2154 | No |
| | (101 by 101) | 81 | – No | 66 | 9444 | No | 74 | 9776 | No | 74 | 9781 | No |
| | (151 by 151) | 80 | – No | 67 | 17797 | No | 39 | 25938 | Yes | 40 | 25881 | Yes |
| 6 | (51 by 51) | 78 | – No | 69 | 2070 | No | 65 | 2188 | No | 65 | 2189 | No |
| | (101 by 101) | 80 | – No | 47 | 8412 | No | 37 | 9332 | Yes | 37 | 9337 | Yes |
| | (151 by 151) | 84 | – No | 49 | 23201 | Yes | 39 | 25764 | Yes | 40 | 25732 | Yes |
| 7 | (51 by 51) | 78 | – No | 65 | 2092 | No | 64 | 2143 | No | 65 | 2188 | No |
| | (101 by 101) | 80 | – Yes | 41 | 8830 | Yes | 39 | 9324 | Yes | 39 | 9341 | Yes |
| | (151 by 151) | 82 | – Yes | 47 | 22219 | Yes | 46 | 24672 | No | 45 | 24776 | No |
| 8 | (51 by 51) | 77 | – No | 42 | 2001 | Yes | 42 | 2172 | No | 42 | 2172 | No |
| | (101 by 101) | 83 | – No | 79 | 7850 | No | 81 | 9814 | No | 82 | 9829 | No |
| | (151 by 151) | 82 | – No | 47 | 24419 | No | 39 | 25882 | No | 40 | 25826 | Yes |
| 9 | (51 by 51) | 77 | – Yes | 40 | 2094 | No | 41 | 2179 | Yes | 41 | 2182 | No |
| | (101 by 101) | 81 | – No | 64 | 8660 | No | 67 | 9084 | No | 70 | 9395 | No |
| | (151 by 151) | 80 | – No | 77 | 17443 | No | 47 | 25334 | Yes | 45 | 25762 | Yes |
| 10 | (51 by 51) | 80 | – Yes | 64 | 2125 | No | 65 | 2191 | No | 65 | 2196 | No |
| | (101 by 101) | 81 | – No | 52 | 8277 | Yes | 39 | 9317 | Yes | 39 | 9325 | No |
| | (151 by 151) | 81 | – No | 85 | 17839 | No | 79 | 21588 | No | 81 | 21784 | No |

following columns for different numbers of cycles. In Table 5, the first refinement method was used exclusively, in Table 6, the results are shown for the second routine and Table 7 shows the results if the two routines are alternated every cycle (this is referred to as method three).

These results show the importance of the dimension of the matrix and the number of cycles. A large number of cycles is needed, especially when large matrices are considered and using method one. Another important conclusion that can be drawn is that the SSNE is a good indication of the quality of a phase set. This is most evident for large matrices using method three. Table 8 shows the average magnitude of the entries in the matrices and the distribution of the reflections. In column 3, the number of strong independent reflections that are used to calculate the phase error is given. Column 4 contains the total number of independent reflections. In column 5, the number of symmetry-equivalent reflections is given. The numbers are for the upper triangle of the matrix only.

Finally, the use of *a priori* information was examined. In the previous section, the properties of eigendensities suggested they might be used to introduce known information into the process of generating phase sets

using eigenvalues and eigenvectors. In practice, a modified version of method one was used. After generating the eigenvalues and eigenvectors, several contributing eigenvectors were replaced by a contribution from a known atomic position. This was accomplished by replacing the contribution from the Fourier transform from the eigenvector by a contribution from an atom whose position is known. Thus, instead of adding a term from (2) towards the new Karle–Hauptman matrix, the contribution is taken from

$$KH_{h,k_j} = z_j \exp[2\pi i \mathbf{H}(\mathbf{h}_k - \mathbf{h}_h) \cdot \mathbf{r}_j], \quad (4)$$

where \mathbf{r}_j is the position of the known atom and z_j corresponds to its electron density. The contribution is scaled by requiring that the elements KH_{h,h_j} are equal to the corresponding element in the original contribution from (2).

It was found that this procedure results in much faster convergence and that the resultant phase set was nearly independent of the value of the random phases in the starting set. All resulting phase sets had an average phase error lower than 40° when four known atoms were used in the procedure. The conclusion that can be drawn from these results is that use of *a priori*

Table 7. Results of methods one and two combined

The number of cycles indicates how many times either method was applied. The results for each number of cycles are given in three columns. The first column gives the average error in the phase set, the second the SSNE and the third column indicates whether *AUTOFOUR* was able to solve the structure with the phase set produced.

| Phase set | | 0 cycles | | | 50 cycles | | | 500 cycles | | | 2000 cycles | | |
|-----------|--------------|----------|--------|-----|-----------|-------|-----|------------|-------|-----|-------------|-------|-----|
| 1 | (51 by 51) | 80 | 13.58 | No | 62 | 1.85 | No | 44 | 0.52 | Yes | 44 | 0.52 | Yes |
| | (101 by 101) | 79 | 54.04 | Yes | 67 | 8.47 | No | 38 | 3.75 | Yes | 37 | 3.79 | Yes |
| | (151 by 151) | 81 | 132.27 | No | 55 | 21.53 | Yes | 44 | 13.05 | Yes | 43 | 12.86 | Yes |
| 2 | (51 by 51) | 79 | 12.95 | No | 57 | 0.93 | Yes | 43 | 0.48 | Yes | 43 | 0.48 | Yes |
| | (101 by 101) | 81 | 59.58 | No | 53 | 8.55 | Yes | 41 | 3.65 | Yes | 40 | 3.79 | Yes |
| | (151 by 151) | 80 | 129.33 | No | 56 | 23.70 | Yes | 38 | 11.75 | Yes | 38 | 12.11 | Yes |
| 3 | (51 by 51) | 78 | 14.47 | No | 64 | 2.11 | Yes | 40 | 0.48 | Yes | 40 | 0.48 | Yes |
| | (101 by 101) | 79 | 61.20 | Yes | 69 | 8.84 | Yes | 41 | 3.82 | Yes | 40 | 3.79 | Yes |
| | (151 by 151) | 81 | 119.13 | Yes | 52 | 38.72 | No | 45 | 13.58 | No | 43 | 12.81 | Yes |
| 4 | (51 by 51) | 79 | 13.53 | Yes | 69 | 0.89 | No | 67 | 0.52 | No | 66 | 0.52 | No |
| | (101 by 101) | 79 | 58.64 | No | 75 | 9.37 | Yes | 72 | 5.19 | No | 72 | 5.22 | No |
| | (151 by 151) | 83 | 125.70 | Yes | 66 | 39.34 | Yes | 44 | 14.87 | Yes | 43 | 12.84 | Yes |
| 5 | (51 by 51) | 77 | 17.42 | No | 68 | 0.82 | No | 65 | 0.52 | No | 65 | 0.52 | No |
| | (101 by 101) | 81 | 58.77 | No | 63 | 8.76 | No | 72 | 5.27 | No | 72 | 5.22 | No |
| | (151 by 151) | 80 | 126.96 | No | 75 | 37.32 | Yes | 40 | 13.11 | Yes | 39 | 12.88 | Yes |
| 6 | (51 by 51) | 78 | 10.82 | No | 72 | 1.01 | Yes | 65 | 0.52 | No | 65 | 0.52 | No |
| | (101 by 101) | 80 | 57.83 | No | 48 | 10.77 | No | 38 | 3.76 | Yes | 37 | 3.79 | Yes |
| | (151 by 151) | 84 | 123.61 | No | 56 | 25.54 | Yes | 43 | 11.77 | Yes | 42 | 12.12 | Yes |
| 7 | (51 by 51) | 79 | 13.83 | No | 71 | 1.13 | No | 65 | 0.52 | No | 65 | 0.52 | Yes |
| | (101 by 101) | 80 | 59.24 | Yes | 43 | 6.39 | Yes | 40 | 3.78 | Yes | 40 | 3.79 | Yes |
| | (151 by 151) | 82 | 124.99 | Yes | 56 | 30.88 | No | 42 | 13.47 | Yes | 38 | 12.09 | Yes |
| 8 | (51 by 51) | 76 | 14.39 | No | 41 | 0.69 | Yes | 58 | 0.53 | Yes | 65 | 0.52 | No |
| | (101 by 101) | 83 | 51.46 | No | 81 | 10.22 | No | 81 | 5.11 | No | 81 | 5.14 | No |
| | (151 by 151) | 82 | 123.96 | Yes | 54 | 17.45 | Yes | 41 | 12.71 | Yes | 38 | 12.10 | Yes |
| 9 | (51 by 51) | 77 | 13.13 | Yes | 44 | 0.60 | Yes | 41 | 0.52 | Yes | 41 | 0.52 | No |
| | (101 by 101) | 81 | 49.00 | Yes | 66 | 7.40 | No | 67 | 6.73 | No | 68 | 7.40 | No |
| | (151 by 151) | 80 | 136.77 | Yes | 80 | 44.99 | No | 79 | 26.78 | No | 43 | 12.84 | Yes |
| 10 | (51 by 51) | 80 | 12.85 | No | 64 | 1.36 | No | 66 | 0.52 | Yes | 67 | 0.52 | No |
| | (101 by 101) | 81 | 53.42 | No | 66 | 10.06 | No | 40 | 3.87 | No | 40 | 3.79 | Yes |
| | (151 by 151) | 81 | 118.41 | No | 83 | 32.70 | No | 80 | 16.97 | No | 79 | 16.99 | No |

Table 8. Properties of the matrices

| Order of matrix | Average E | No. of strong reflections | No. of independent reflections | Total No. of reflections |
|-----------------|------------|---------------------------|--------------------------------|--------------------------|
| 51 | 1.35 | 191 | 345 | 789 |
| 101 | 1.18 | 328 | 782 | 3774 |
| 151 | 1.10 | 356 | 937 | 9230 |

information is possible but that the nature of the refinement effectively results in a single solution method.

5. Conclusions

The eigenvalues of a large Karle-Hauptman matrix can be used for several purposes. First of all, they provide information about the quality of the phase set. Large negative eigenvalues indicate there is little relation between the phase set and the crystal structure.

Second, the eigendensities provide a means to write the Karle-Hauptman matrix as the sum of the contribution of the eigenvalues. Therefore, eigendensities can be used to put known structural information into a

Karle-Hauptman matrix simply by exchanging one eigenvalue and eigenvector from the random starting set with one calculated from a known atomic position.

Finally, the eigenvalues can be used in phase refinement, for example using the methods described in the previous section. The overall conclusion is that the results are promising but the calculations are time consuming and considerable research is still needed in this area. Further investigation is being performed on combining these techniques with the 'shake-and-bake' principle, which has become popular recently.

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