

## Wrong Symmetry – Don't get 'Marshed'

Apart from simple error, there are other reasons for applying the wrong symmetry:

1. Space group ambiguity due to degenerate systematic absences. (eg Pnma, Pna2<sub>1</sub>)
2. Deliberate choice of a lower symmetry space group to facilitate structure solution by direct methods.

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## Lowering Symmetry

Sometimes, a good set of data for a crystal in a centro-symmetric space group fails to solve by Direct Methods.

What can be tried?

1. Reading the manual
2. A different program.

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## Lowering Symmetry

Another solution is to try a related non-centro symmetric space group.

P-1 => P1

P2<sub>1</sub>/c => P2<sub>1</sub>

C2/c => C2

If the structure now solves, don't be fooled into believing that the low symmetry SG is necessarily the correct one. Convert the structure back to the original SG if possible.

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## Refinement Implications

The related moieties in a structure refined in a space group of too-low symmetry may appear to be so different that the analyst is convinced they really are different.

If the missing symmetry is a centre of symmetry or a translation, the situation is particularly serious due to correlation in the normal matrix.

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## What are the Symptoms?

The most evident symptom is usually strange values for physical parameters, eg unusual bond lengths or weird adps.

However, the average of the pseudo-symmetrically related quantities is often quite reasonable, one bond is long and the other short, one adp is tiny and the other massive.

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## What can be done?

Always try the more symmetric space group.

If the pseudo-operator involves translation, look again at the systematic absences.

If the R factors are similar, look at the agreement of the low angle weak reflections.

If the geometry generally improves in the more symmetric SG, but some disorder is introduced, consider publishing the structure with a suitable comment.

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## What can be done?

If you decide to stay with the lower symmetry, take care!

In the extreme case, the normal matrix will become singular (zero determinant). This can be concealed or treated in several ways:

1. Use of an augmented diagonal (Marquardt method)
2. Use of partial shifts.
3. Blocked matrix. This is almost NEVER acceptable

*Methods 1 & 2 may be built into your program so that you may not realise that you have a problem*

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## Demo – Solution of Simultaneous Equations

$$\begin{bmatrix} 3 & 6 \\ 4 & 2 \end{bmatrix} \cdot \begin{bmatrix} x \\ y \end{bmatrix} = \begin{bmatrix} 21 \\ 22 \end{bmatrix}$$

(ask for volunteer to solve these equations)

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## Try solving 2 more simultaneous equations

$$\begin{bmatrix} 3 & 6 \\ 2 & 4 \end{bmatrix} \cdot \begin{bmatrix} x \\ y \end{bmatrix} = \begin{bmatrix} 21 \\ 14 \end{bmatrix}$$

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## Try Solving by Least Squares

$$\begin{bmatrix} 3 & 2 \\ 6 & 4 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix} = \begin{bmatrix} 3 & 2 \\ 6 & 4 \end{bmatrix} \begin{bmatrix} 21 \\ 14 \end{bmatrix}$$

$$\begin{bmatrix} 13 & 26 \\ 26 & 52 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix} = \begin{bmatrix} 91 \\ 182 \end{bmatrix}$$

Note the determinant is zero

(Don't bother with a volunteer – the problem is evident) 10

## Try Blocking the Matrix (Dropping the off-diagonal terms)

$$\begin{bmatrix} 13 & \\ & 52 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix} = \begin{bmatrix} 91 \\ 182 \end{bmatrix}$$

Yielding  $x=7.0$ ,  $y=3.5$

Substitute these into original equation

$$\begin{array}{rcl} 3x & + & 6y = 21(obs) \\ 3 \times 7.0 & + & 6 \times 3.5 = 42(calc) \end{array}$$

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## The Real Answer

$$\begin{bmatrix} 3 & 6 \\ 2 & 4 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix} = \begin{bmatrix} 21 \\ 14 \end{bmatrix}$$

By inspection,  $x=5$ ,  $y=1$  is a better fit

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## Lowering Symmetry

*This set of images was made from an old set of 35 mm slides.*

Originally designed to show the pit-falls associated with lowering space group symmetry, they also show techniques that could be use in other difficult situations.

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## Lowering Symmetry

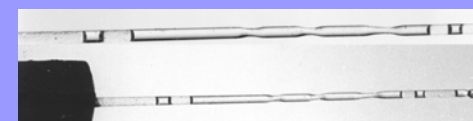
In cases where the systematic absences do not unambiguously define the space group, the recommended strategy is to start with the space group of highest reasonable symmetry.

If the structure looks generally correct, but the refinement appears unsatisfactory, refinements could be tried in less symmetrical space groups – but be prepared for problems.

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## Lowering Symmetry. A contrived example

This example is based upon the real structure of 1,4 dimethylcyclohexane. This is a liquid, but can be crystallised in a Lindeman tube at low temperatures. When the work was done, in 1979, the use of Weissenberg geometry diffractometers made it easy to mis-judge (or miss altogether) the systematic absences.



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## Lowering Symmetry. Problems

In this case, an approximate solution was found in the higher symmetry SG, ( $P2_1/c$ ) but did not refine.

A low-symmetry refinement can be started from a high-symmetry approximation by changing the space group and adding atoms symmetrically related to those already found.

However, unless care is taken, the refinement will 'blow up'.

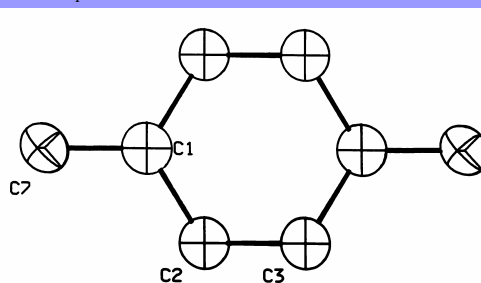
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## Initial refinement in $P2_1/c$

The asymmetric unit is  $\frac{1}{2}$  molecule.  $R=18.7\%$

$C1-C7=1.41$ , all others  $1.52$

$U_i$  for C7 are 0.038, 0.050, 0.649



## Try Lowering the symmetry

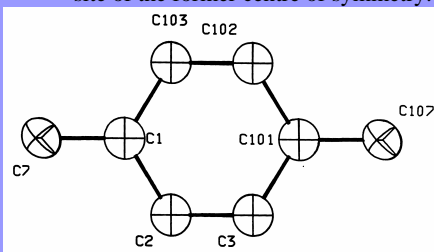
The refinement in  $P2_1/c$  has got bogged down. This may be due to really poor data, or to a mis-assignment of the space group.

Try lowering the symmetry from  $P2_1/c$  to  $P2_1$

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## Continue refinement in $P2_1$

The asymmetric unit is now a whole molecule lying on the site of the former centre of symmetry.



CRYSTALS INSTRUCTION: CREATE 100 FIRST(-1) UNTIL LAST

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## The Seeds of Despair

The new structure consists of twice as many atoms as the original.

They are in pairs related by the former centre of symmetry, which has been eliminated by changing the space group.

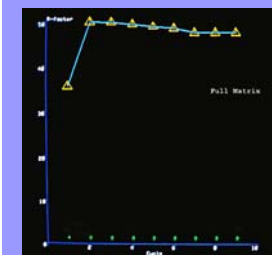
Because the atoms are still centrosymmetrically related, the calculated structure factors (and hence R) are the same as before.

However, the least squares matrix has twice as many variables as before.

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## Try Full Matrix refinement

Starting from a centro symmetric model in a non-centro space group, the refinement immediately 'blows up'. R rises to 50%, with bond lengths in range 0.69 to 1.78

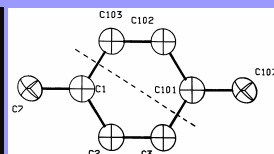
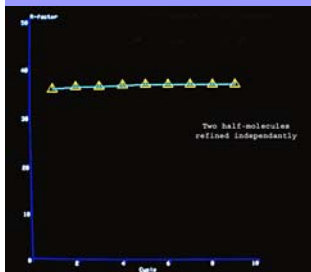


CRYSTALS INSTRUCTIONS:  
FULL X'S

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## Refine the two halves separately

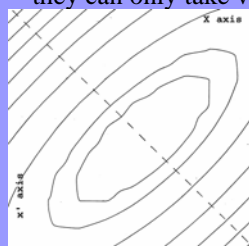
This can be done either by refining alternate half molecules in alternate cycles, or by a block-diagonal matrix. R rises to 37%, with bond lengths in range 1.39 to 1.53.



CRYSTALS INSTRUCTIONS:  
BLOCK C(1,X'S) UNTIL C(7)  
BLOCK C(101,X'S) UNTIL C(107)

## Minimisation Surfaces

Contours of constant value of the residual.  $x$  and  $x'$  are allowed to vary while all other parameters are held fixed. If  $x$  and  $x'$  are related by symmetry, they can only take values lying on the diagonal line.

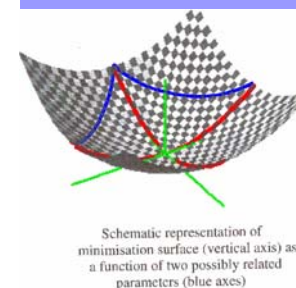


The minimum is well defined in this direction. If  $x$  and  $x'$  are allowed to vary independently, the minima is less well defined.

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## Minimisation Surfaces

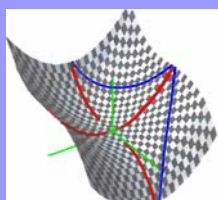
Perspective representation of a minimisation surface which remains stable even when symmetry is relaxed. Remember that this surface assumes that all other parameters are held constant.



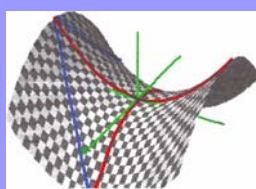
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## Minimisation surfaces

Other possible minimisation surfaces. If the gradient perpendicular to the symmetry line is very acute, massive parameter shifts can occur. Note that after the next cycle the surfaces may be quite different because of shifts in the other parameters.



Schematic representation of minimisation surface (vertical axis) as a function of two possibly related parameters (blue axes)



Schematic representation of minimisation surface (vertical axis) as a function of two possibly related parameters (blue axes)

## Stabilising the refinement

It is highly likely that when the symmetry is reduced, the singularity or near singularity in the normal matrix (which is computed from the symmetric model) will lead to nonsense parameter shifts, and the model will fail to refine.

Remember that we do not observe the terms in the Normal Matrix.  
We compute them from the current model

What can be done?

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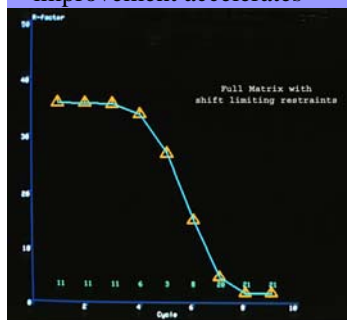
## Stabilising the Refinement

If, by chance, enough parameters move a small amount in the correct direction, the pseudo-symmetry may be broken, leading to a matrix giving valid shifts. This can be encouraged with harsh shift-limiting restraints (also known as Marquardt minimisation).

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## Stabilising the refinement

Note that once the model begins to improve, the improvement accelerates



CRYSTALS INSTRUCTIONS:  
LIMIT 0.005 X  
LIMIT 0.005 Y  
LIMIT 0.005 Z 28

## Stabilising the refinement

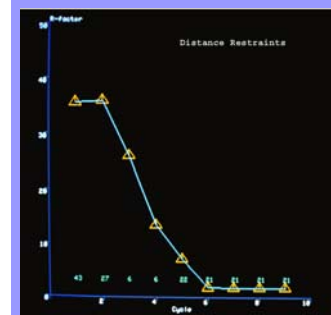
Hoping that random shifts will eventually lead to a more valid model becomes less likely for larger structures.

The chance of stabilising the refinement can be increased by putting information into the calculation.

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## Distance restraints

Our knowledge of the structure of hydrocarbons enables us to predict bond lengths of about 1.54Å

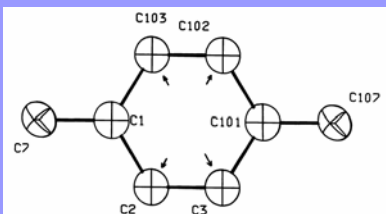


Recall that C1-C7 was too short. Suggest a reasonable value.

CRYSTALS INSTRUCTIONS:  
DIST 1.54,.01 =C(1) TO C(7)  
CONT C(101) TO C(107)  
etc 30

## Molecular Symmetry

The central ring looks more or less OK, so let it relax but preserve the symmetry.

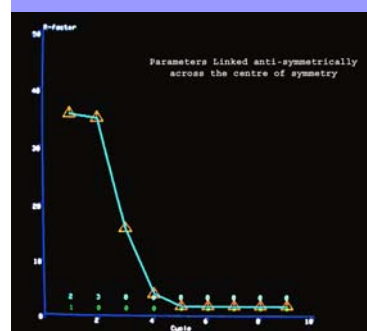


CRYSTALS INSTRUCTIONS:  
FULL X'S  
LINK C(1,X'S) UNTIL C(3) AND  
CONT C(101,X'S) UNTIL C(103)  
WEIGHT -1 C(101,X'S) UNTIL C(103)

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## Molecular Symmetry

This converges rapidly because the information content of the constraint is high.



The constraints should be removed for the final refinement

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## Understanding of the Maths

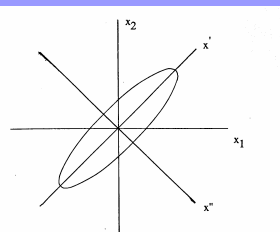
The nature of the instability on reducing the symmetry is well understood. Pairs of symmetrically related parameters are highly correlated.

A technique made popular in environmental statistics is to re-parameterise the problem in terms of less correlated parameters.

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## Orthogonal Parameters

New parameters can be defined which are (almost) orthogonal, and thus uncorrelated.



Edward Prince, Mathematical Techniques in Crystallography.

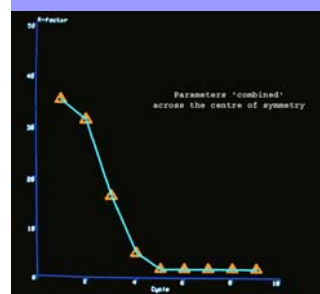
$$x' = x_1 + x_2$$

$$x'' = x_1 - x_2$$

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## Orthogonal Parameters

Using the new parameters, the refinement quickly converges. Very slack shift limiting restraints were added as a precaution.



CRYSTALS INSTRUCTIONS  
COMBINE C(1,X'S) UNTIL C(7)  
CONT AND C(101,X'S) UNTIL LAST  
LIMIT 1.0 X  
LIMIT 1.0 Y  
LIMIT 1.0 Z

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## Rigid Group Refinement

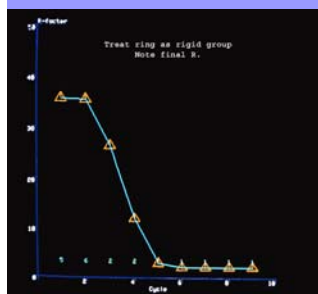
If the central ring looks good enough, we can refine it as a rigid group (ie refine its centroid and orientation).

The errant C7 and C107 atoms will need to be refined independently. They are re-parameterised to orthogonal coordinates.

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## Rigid Group Refinement

Convergence is rapid, but the final R factor is higher than in a free refinement. The GROUP constraint needs removing for the final refinement.



CRYSTALS INSTRUCTIONS  
GROUP C(1) UNTIL C(3)  
CONT C(101) UNTIL C(103)  
COMBINE C(7,X'S) AND C(107,X'S)

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## Summary of Results to Date

Full matrix simply blows away and never converges.

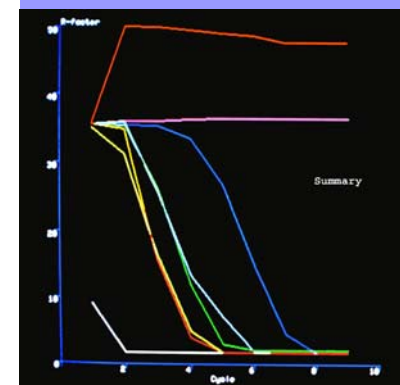
Refining half-structures shows no improvement.

Harsh shift limiting restraints get there in the end.

Methods which use external information converge most rapidly.

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## Summary of Results to Date



The relative success of the different techniques will vary from case to case.

There is a technique which we have not looked at so far, represented by the white curve.

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## I know nothing

The previous examples are using our knowledge of the normal geometry of alkanes.

What can we do if the structure is novel?

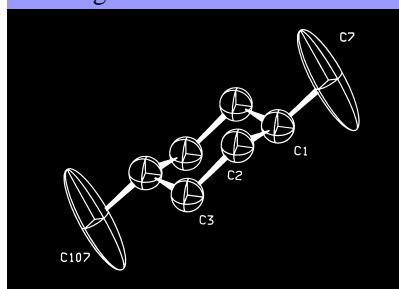
If the trial structure is not completely implausible, we can fiddle the maths.

1. Apply harsh shift limiting (Marquardt) restraints.
2. Only use part of the computed shift.
3. Set maximal values for parameter shifts.

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## Pay Attention!

The 'adps' are sometimes regarded as a waste-bin for errors. In difficult cases, it might be worth sorting through the rubbish.



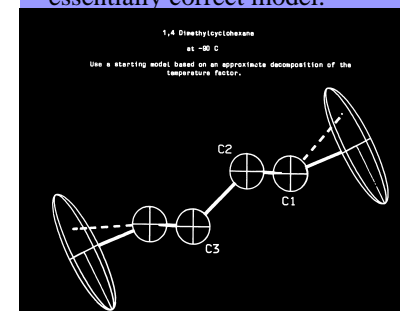
Original centro-symmetric anisotropic refinement.

The methyl groups look pretty unrealistic.

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## Postulate a Solution

If the structure looks wrong, try to postulate a feasible solution. Remember that LS can only improve an essentially correct model.



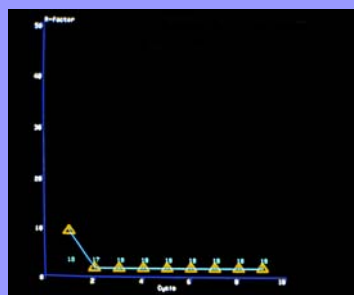
Instead of starting the low-symmetry refinement with atoms at the centre of the ellipsoids, we can choose non-symmetric sites from each end of the ellipsoid.

We have broken the symmetry manually.

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## Given the correct start .....

With this guess at the structure, the initial R-factor is much lower than the centro-symmetric case, and convergence is almost immediate.



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## Conclusion

There is no real substitute for a good model and additional external information or hypotheses.

The mathematical techniques for bounding shifts, taking partial shifts or augmenting the diagonal of the normal matrix are essential for difficult cases, but should not be the techniques of first-resort.

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## Exercises

Look at questions  
4, 26, 29, 17

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