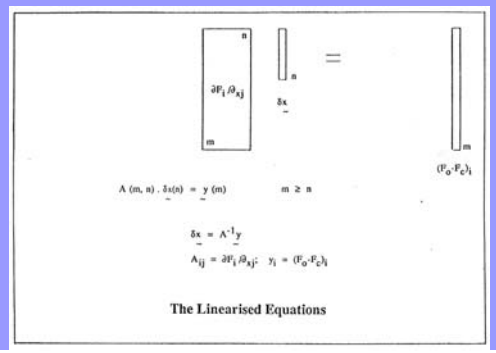
Anatomy of a Least Squares Program

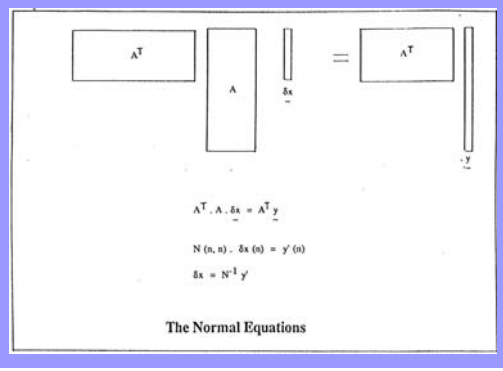
Most small molecule refinement programs have the same underlying anatomy. The calculations are carried out in crystal fractions.

RAELS, by David Rae, is probably unique by working in an orthogonal coordinate system.

The design matrix, unknown shifts and vector of residuals



The product $A^T.A$ is the square Normal matrix Note that A_TA is smaller than A



Constraints

Constraints are conditions which **MUST** be obeyed. They represent concepts or information which is not subject to any doubt.

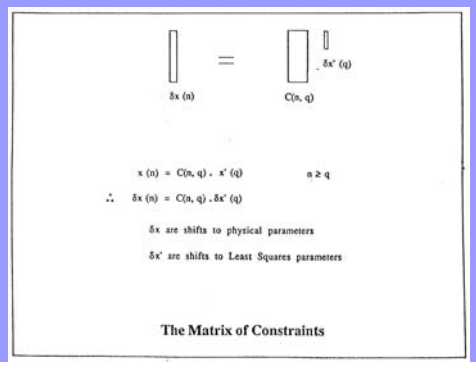
Examples are relationships between parameters for atoms on special positions, for 'riding' parameters, geometrically rigid entities, and thermal rigid bodies.

Equations of Constraint

The physical ('real') parameters are related to a smaller set of least squares parameters together with some additional, unconditional, knowledge.

$$[physical\ parameters] = [knowledge][LS\ parameters]$$

The matrix of constraint relates the physical parameters to a smaller set of LS parameters.



Matrix of constraint

Atom on special position (*x*,-*x*,*z*) requires only 2 LS parameters

$$\begin{bmatrix} x \\ -x \\ z \end{bmatrix} = \begin{bmatrix} 1 & 0 \\ -1 & 0 \\ 0 & 1 \end{bmatrix} . \begin{bmatrix} u \\ v \end{bmatrix}$$

Matrix of constraint

Atom on special position (*x*,2*x*,*z*) requires only 2 LS parameters.

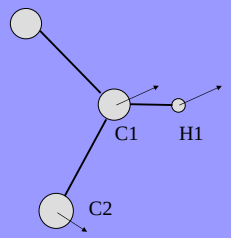
$$\begin{bmatrix} x \\ 2x \\ z \end{bmatrix} = \begin{bmatrix} 1 & 0 \\ 2 & 0 \\ 0 & 1 \end{bmatrix} . \begin{bmatrix} u \\ v \end{bmatrix}$$

Matrix of Constraint

'Riding' a hydrogen atom on a carbon atom is done via the matrix of constraint.

$$\begin{bmatrix} C\delta x \\ C\delta y \\ C\delta z \\ H\delta x \\ H\delta y \\ H\delta z \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} . \begin{bmatrix} \delta x \\ \delta y \\ \delta z \end{bmatrix}$$

Riding Hydrogen



C1 and H1 move synchronously, preserving the bond length and direction.

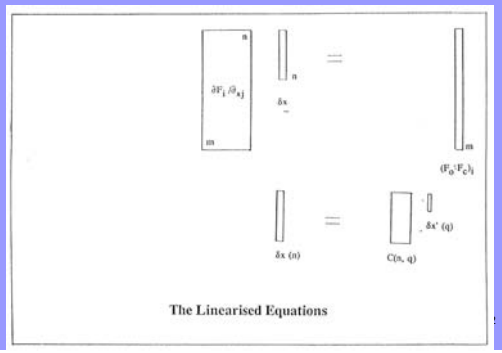
C3 moves independently, perturbing the C2-C1-H1 angle

Matrix of constraint Rigid Body Refinement

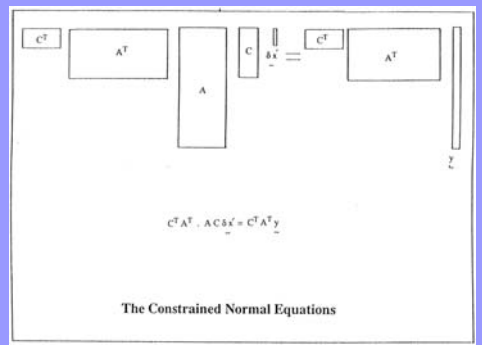
3 atoms in a rigid group. The 9 atomic parameters are represented by 6 LS parameters

$$\begin{bmatrix} x_1 \\ y_2 \\ z_1 \\ x_2 \\ y_1 \\ z_2 \\ x_3 \\ y_3 \\ z_3 \end{bmatrix} = \begin{bmatrix} 1 & & & \frac{\partial x}{\partial \theta} & \frac{\partial x}{\partial \phi} & \frac{\partial x}{\partial \chi} \\ & 1 & & \frac{\partial y}{\partial \theta} & \cdot & \cdot \\ & & 1 & \cdot & \cdot & \cdot \\ 1 & & & \cdot & \cdot & \cdot \\ & 1 & & \cdot & \cdot & \cdot \\ & & 1 & \cdot & \cdot & \cdot \\ 1 & & & \cdot & \cdot & \cdot \\ & 1 & & \cdot & \cdot & \cdot \\ & & 1 & \frac{\partial z_3}{\partial \theta} & \frac{\partial z_3}{\partial \varphi} & \frac{\partial z_3}{\partial \chi} \end{bmatrix} \cdot \begin{bmatrix} u \\ v \\ w \\ \theta \\ \varphi \\ \chi \end{bmatrix}$$

The matrix of constraint can be inserted into the Normal equations



Note that the product $C^TA^T.A\,C$ is smaller than the original Normal matrix.

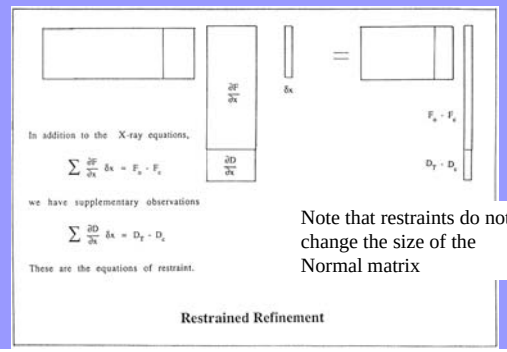


Restraints

Restraints are conditions which are believed (or hoped) to be correct. They are often based on previous experiments, and sometimes called 'prior' or 'Bayesian' information. They are introduced into the calculation in such a way that they can be over-ridden if they seem inappropriate.

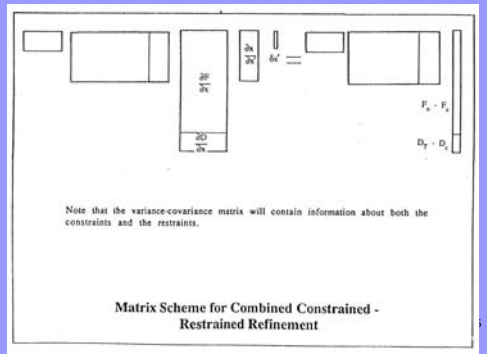
Examples are: Bond lengths & Angles, Geometrical or adp similarity, pseudo-symmetry conditions, non-bonded repulsions.

Restraining information is added as auxilliary observations to the Design matrix and residual.



Note that restraints do not change the size of the Normal matrix

Put all the bits together. We still have to consider weights and damping.



Damping refinements

Damping is introduced to control unrealistic parameter shifts. There are two methods

1. Partial shifts. The parameter shifts found by the LS are multiplied by some factor, generally less than unity.
2. Shift limiting restraints (modified Marquardt method). The diagonal elements of the normal matrix are augmented.

Partial Shift Factors

$$\delta x' = P.\delta x$$

$\boldsymbol{\delta x'}$ is the applied shift, $\boldsymbol{P}$ is the diagonal matrix of partial shift factors.

They may be given absolute values, or set to scale the largest shift to some value.

Shift Limiting Restraints

We use the pseudo-observation that the new parameter should be the same as the old parameter. This equation must be weighted in the usual way.

$$x_o = x$$

$$x_o = x_c + \frac{\partial x_c}{\partial x} . \delta x$$

Problems with damping

Partial shifts are applied after inversion. If the matrix is almost singular, very large shifts can still occur. Maximal shift boundaries are often also applied.

Shift limiting restraints are applied to the matrix before inversion, so are generally well-behaved. They will reduce the apparent parameter uncertainties.

Reflection Weights

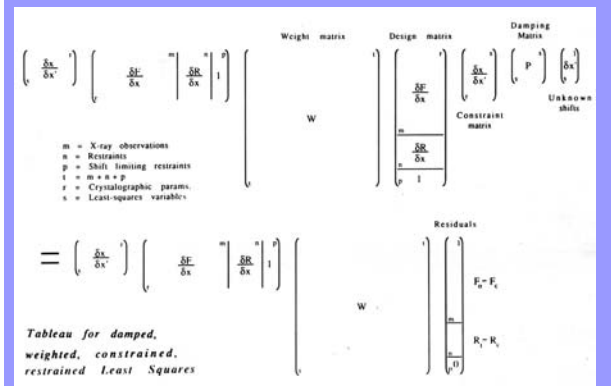
There is an uncertainty attached to the value of every observed structure factor.

Reflections with large uncertainty should be given less importance – down weighted.

If one really knew the variance of a reflection, its weight would be $w = 1/\sigma^2(observation)$

The uncertainties in the values of reflections are probably correlated, so that the covariances of reflections should also be considered in the Weight Matrix

The total scheme



Floating Origins

There are many space groups where the origin in one or more directions can be chosen quite arbitrarily – *e.g.* $P2_1$, Pm, P1.

For such cases the Normal matrix for least squares on all positional parameters will be singular and cause chaos unless special care is taken:

Floating Origins - Poor Remedies

Use a matrix-invertor which will 'trap' the singularity – the Cholesky method

Manually omit the appropriate coordinates of one atom from the refinement.

Floating Origins - Better Solutions

Use Shift limiting restraints.

Use Centroid-fixing restraints.

$$\sum^{atoms} w_i y_i = \text{constant}$$

Use a matrix-invertor which will eliminate the singularity – eigen value filtering

Chapter 12 Exercises

Look at questions

1, 2, 3, 5, 27, 28