$$\mathbf{J} = \begin{bmatrix} \dfrac{\partial F_1}{\partial \rho_1} & \dfrac{\partial F_1}{\partial \rho_2} & \cdots & \dfrac{\partial F_1}{\partial \rho_n} \\ \dfrac{\partial F_2}{\partial \rho_1} & \dfrac{\partial F_2}{\partial \rho_2} & \cdots & \dfrac{\partial F_2}{\partial \rho_n} \\ \vdots & \vdots & \ddots & \vdots \\ \dfrac{\partial F_m}{\partial \rho_1} & \dfrac{\partial F_m}{\partial \rho_2} & \cdots & \dfrac{\partial F_m}{\partial \rho_n} \end{bmatrix}, \tag{15.1.5.5}$$

ε is a vector of residuals to equation (15.1.5.3) for a trial solution, $\rho(\mathbf{x})$, and $\delta\rho(\mathbf{x})$ is a vector of shifts to the density. Hence, the solution for $\rho(\mathbf{x})$ is achieved in an iterative manner,

$$\rho^{i+1}(\mathbf{x}) = \rho^{i}(\mathbf{x}) + \delta\rho(\mathbf{x}). \tag{15.1.5.6}$$

Therefore, the problem of solving a system of nonlinear equations (15.1.5.3) is transformed into solving a system of linear equations (15.1.5.4), which forms one cycle of Newton–Raphson iteration.

If there are more equations than unknowns ($m > n$), the unknowns are obtained through a least-squares solution to equations (15.1.5.4),

$$\mathbf{J}^T\mathbf{J}\delta\rho(\mathbf{x}) = -\mathbf{J}^T\varepsilon. \tag{15.1.5.7}$$

Theoretically, the above system of equations could be solved by matrix multiplication and inversion, *i.e.*

$$\delta\rho(\mathbf{x}) = -\left(\mathbf{J}^T\mathbf{J}\right)^{-1}\mathbf{J}^T\varepsilon. \tag{15.1.5.8}$$

However, the amount of calculation involved in setting up the normal matrix of least squares is huge for the problem presented by protein structures. This can be completely avoided by using the conjugate-gradient technique for solving the system of linear equations.

15.1.5.2.1. *The conjugate-gradient method*

The conjugate-gradient method does not require the inversion of the normal matrix, and therefore the solution to a large system of linear equations can be achieved very quickly.

Starting from a trial solution to equations (15.1.5.4), such as a null vector,

$$\delta\rho_0(\mathbf{x}) = \mathbf{0}, \tag{15.1.5.9}$$

the initial residual is

$$\mathbf{r}_0 = -\mathbf{J}^T(\varepsilon - \mathbf{J}\delta\rho_0(\mathbf{x})) \tag{15.1.5.10}$$

and the initial search step is

$$\mathbf{p}_0 = \mathbf{r}_0. \tag{15.1.5.11}$$

The iterative process is as follows. The new shift to the density is

$$\delta\rho_{k+1}(\mathbf{x}) = \delta\rho_k(\mathbf{x}) + \alpha_k\mathbf{p}_k, \tag{15.1.5.12}$$

where

$$\alpha_k = \mathbf{r}_k^T\mathbf{p}_k/\mathbf{q}_k^T\mathbf{q}_k \tag{15.1.5.13}$$

and

$$\mathbf{q}_k = \mathbf{J}\mathbf{p}_k. \tag{15.1.5.14}$$

The new residual is

$$\mathbf{r}_{k+1} = \mathbf{r}_k - \alpha_k\mathbf{s}_k, \tag{15.1.5.15}$$

where

$$\mathbf{s}_k = \mathbf{J}^T\mathbf{q}_k. \tag{15.1.5.16}$$

The next search step which conjugates with the residual is

$$\mathbf{p}_{k+1} = \mathbf{r}_{k+1} + \beta_k\mathbf{p}_k, \tag{15.1.5.17}$$

where

$$\beta_k = -\mathbf{r}_{k+1}^T\mathbf{s}_k/\mathbf{q}_k^T\mathbf{q}_k. \tag{15.1.5.18}$$

The process is iterated by increasing k until convergence is reached, when

$$|\mathbf{r}_{k+1} - \mathbf{r}_k| \Rightarrow 0.$$

The number of iterations required for an exact solution is equal to the number of unknowns, because the search vector at each step is orthogonal with all the previous steps. However, a very satisfactory solution can normally be reached after very few iterations. This makes the conjugate-gradient method a very efficient and fast procedure for solving a system of equations. Note that the normal matrix never appears explicitly, although it is implicit in (15.1.5.10) and (15.1.5.16). The inversion of the normal matrix and matrix multiplication is completely avoided. Most of the calculation comes from the formation of the matrix-vector products in (15.1.5.10), (15.1.5.14), and (15.1.5.16). These can be expressed as convolutions and can be performed using FFTs, thus saving considerably more time.

The solution to $\delta\rho(\mathbf{x})$ at the end of conjugate-gradient iteration is substituted into equation (15.1.5.6) to get a new solution for $\rho(\mathbf{x})$. The solution to the system of nonlinear equations (15.1.5.3) is obtained when the Newton–Raphson iteration has reached convergence.

15.1.5.2.2. *The full-matrix solution*

The equations to be solved for the electron-density shifts, $\delta\rho(\mathbf{x})$, are from the Jacobian of equation (15.1.5.2),

$$\begin{cases} (2V/N)\sum\limits_{\mathbf{y}}\rho(\mathbf{y})\psi(\mathbf{x}-\mathbf{y}) - \delta\rho(\mathbf{x}) = \Delta\rho(\mathbf{x}) \\ \delta\rho(\mathbf{x}) = \Delta H(\mathbf{x}) \end{cases}, \tag{15.1.5.19}$$

where $\Delta\rho(\mathbf{x})$ is the residual to Sayre's equation,

$$\Delta\rho(\mathbf{x}) = \rho(\mathbf{x}) - (V/N)\sum_{\mathbf{y}}\rho^2(\mathbf{y})\psi(\mathbf{x}-\mathbf{y}), \tag{15.1.5.20}$$

and $\Delta H(\mathbf{x})$ is the residual to the linear density-modification equations,

$$\Delta H(\mathbf{x}) = H(\mathbf{x}) - \rho(\mathbf{x}). \tag{15.1.5.21}$$

Starting from a trial solution of $\delta\rho_0(\mathbf{x}) = \mathbf{0}$, the initial residual vector is

$$\mathbf{r}_0(\mathbf{x}) = (2/V)\rho(\mathbf{x})\sum_{\mathbf{h}}\theta(\overline{\mathbf{h}})\Delta F(\mathbf{h})\exp(-2\pi i\mathbf{h}\mathbf{x}) - \Delta\rho(\mathbf{x}) + \Delta H(\mathbf{x}), \tag{15.1.5.22}$$

where

$$\Delta F(\mathbf{h}) = F(\mathbf{h}) - \theta(\mathbf{h})G(\mathbf{h}), \tag{15.1.5.23}$$

$$G(\mathbf{h}) = (V/N)\sum_{\mathbf{y}}\rho^2(\mathbf{y})\exp(2\pi i\mathbf{h}\mathbf{y}) \tag{15.1.5.24}$$

and

$$\Delta\rho(\mathbf{x}) = (1/V)\sum_{\mathbf{h}}\Delta F(\mathbf{h})\exp(-2\pi i\mathbf{h}\mathbf{x}). \tag{15.1.5.25}$$

Thus, only three FFTs are required to calculate the initial residual. The residual of Sayre's equation is given in equation (15.1.5.23).

The calculation of $\mathbf{q}_k$ in equation (15.1.5.14) is achieved in a similar manner using FFTs,

references