Tironi *et al.* have introduced a generalized reaction field in which the dielectric continuum beyond the cutoff r_c also has an ionic strength I [52]. In this case we can rewrite the constants k_{rf} and c_{rf} using the inverse Debye screening length κ:

$$\kappa^2 = \frac{2I\,F^2}{\varepsilon_0 \varepsilon_{rf} RT} = \frac{F^2}{\varepsilon_0 \varepsilon_{rf} RT} \sum_{i=1}^{K} c_i z_i^2 \tag{4.18}$$

$$k_{rf} = \frac{1}{r_c^3} \frac{(\varepsilon_{rf} - \varepsilon_r)(1 + \kappa r_c) + \frac{1}{2}\varepsilon_{rf}(\kappa r_c)^2}{(2\varepsilon_{rf} + \varepsilon_r)(1 + \kappa r_c) + \varepsilon_{rf}(\kappa r_c)^2} \tag{4.19}$$

$$c_{rf} = \frac{1}{r_c} \frac{3\varepsilon_{rf}(1 + \kappa r_c + \frac{1}{2}(\kappa r_c)^2)}{(2\varepsilon_{rf} + \varepsilon_r)(1 + \kappa r_c) + \varepsilon_{rf}(\kappa r_c)^2} \tag{4.20}$$

where F is Faraday's constant, R is the ideal gas constant, T the absolute temperature, c_i the molar concentration for species i and z_i the charge number of species i where we have K different species. In the limit of zero ionic strength ($\kappa = 0$) eqns. 4.19 and 4.20 reduce to the simple forms of eqns. 4.15 and 4.16 respectively.

4.1.5 Modified non-bonded interactions

In the GROMACS force field the non-bonded potentials can be modified by a shift function. The purpose of this is to replace the truncated forces by forces that are continuous and have continuous derivatives at the cutoff radius. With such forces the time-step integration produces much smaller errors and there are no such complications as creating charges from dipoles by the truncation procedure. In fact, by using shifted forces there is no need for charge groups in the construction of neighbor lists. However, the shift function produces a considerable modification of the Coulomb potential. Unless the 'missing' long-range potential is properly calculated and added (through the use of PPPM, Ewald, or PME), the effect of such modifications must be carefully evaluated. The modification of the Lennard-Jones dispersion and repulsion is only minor, but it does remove the noise caused by cutoff effects.

There is *no* fundamental difference between a switch function (which multiplies the potential with a function) and a shift function (which adds a function to the force or potential) [53]. The switch function is a special case of the shift function, which we apply to the *force function* $F(r)$, related to the electrostatic or Van der Waals force acting on particle i by particle j as

$$\boldsymbol{F}_i = cF(r_{ij})\frac{\boldsymbol{r}_{ij}}{r_{ij}} \tag{4.21}$$

For pure Coulomb or Lennard-Jones interactions $F(r) = F_\alpha(r) = r^{-(\alpha+1)}$. The shifted force $F_s(r)$ can generally be written as:

$$\begin{aligned} F_s(r) &= F_\alpha(r) & r < r_1 \\ F_s(r) &= F_\alpha(r) + S(r) & r_1 \le r < r_c \\ F_s(r) &= 0 & r_c \le r \end{aligned} \tag{4.22}$$

When $r_1 = 0$ this is a traditional shift function, otherwise it acts as a switch function. The corresponding shifted coulomb potential then reads:

$$V_s(r_{ij}) = f\Phi_s(r_{ij})q_i q_j \tag{4.23}$$

where $\Phi(r)$ is the potential function

$$\Phi_s(r) = \int_r^\infty F_s(x)\,dx \tag{4.24}$$

The GROMACS shift function should be smooth at the boundaries, therefore the following boundary conditions are imposed on the shift function:

$$\begin{align}
S(r_1) &= 0 \\
S'(r_1) &= 0 \\
S(r_c) &= -F_\alpha(r_c) \\
S'(r_c) &= -F'_\alpha(r_c)
\end{align} \tag{4.25}$$

A 3rd degree polynomial of the form

$$S(r) = A(r - r_1)^2 + B(r - r_1)^3 \tag{4.26}$$

fulfills these requirements. The constants A and B are given by the boundary condition at r_c:

$$\begin{align}
A &= -\frac{(\alpha + 4)r_c - (\alpha + 1)r_1}{r_c^{\alpha+2}\,(r_c - r_1)^2} \\
B &= \frac{(\alpha + 3)r_c - (\alpha + 1)r_1}{r_c^{\alpha+2}\,(r_c - r_1)^3}
\end{align} \tag{4.27}$$

Thus the total force function is

$$F_s(r) = \frac{\alpha}{r^{\alpha+1}} + A(r - r_1)^2 + B(r - r_1)^3 \tag{4.28}$$

and the potential function reads

$$\Phi(r) = \frac{1}{r^\alpha} - \frac{A}{3}(r - r_1)^3 - \frac{B}{4}(r - r_1)^4 - C \tag{4.29}$$

where

$$C = \frac{1}{r_c^\alpha} - \frac{A}{3}(r_c - r_1)^3 - \frac{B}{4}(r_c - r_1)^4 \tag{4.30}$$

When $r_1 = 0$, the modified Coulomb force function is

$$F_s(r) = \frac{1}{r^2} - \frac{5r^2}{r_c^4} + \frac{4r^3}{r_c^5} \tag{4.31}$$

identical to the *parabolic force* function recommended to be used as a short-range function in conjunction with a Poisson solver for the long-range part [17]. The modified Coulomb potential function is

$$\Phi(r) = \frac{1}{r} - \frac{5}{3r_c} + \frac{5r^3}{3r_c^4} - \frac{r^4}{r_c^5} \tag{4.32}$$
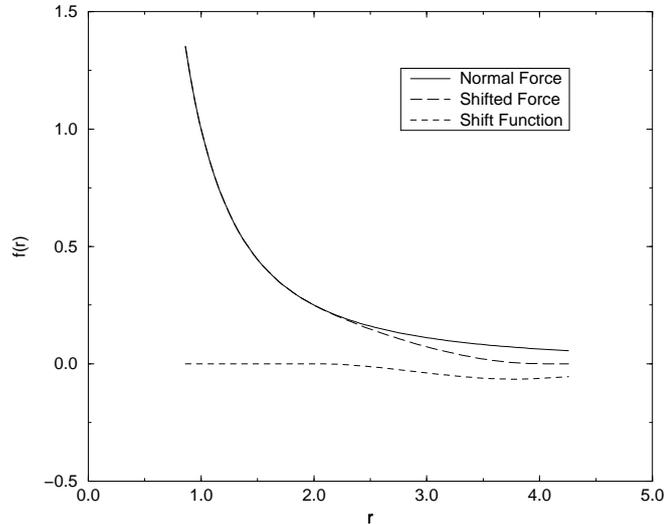
see also Fig. 4.4.

Figure 4.4: The Coulomb Force, Shifted Force and Shift Function $S(r)$, using $r_1 = 2$ and $r_c = 4$.

4.1.6   Modified short-range interactions with Ewald summation

When Ewald summation or particle-mesh Ewald is used to calculate the long-range interactions, the short-range coulomb potential must also be modified, similar to the switch function above. In this case the short range potential is given by

$$V(r) = f\frac{\text{erfc}(\beta r_{ij})}{r_{ij}}q_i q_j, \tag{4.33}$$

where β is a parameter that determines the relative weight between the direct space sum and the reciprocal space sum and $\text{erfc}(x)$ is the complementary error function. For further details on long-range electrostatics, see sec. 4.9.

4.2   Bonded interactions

Bonded interactions are based on a fixed list of atoms. They are not exclusively pair interactions, but include 3- and 4-body interactions as well. There are *bond stretching* (2-body), *bond angle* (3-body), and *dihedral angle* (4-body) interactions. A special type of dihedral interaction (called *improper dihedral*) is used to force atoms to remain in a plane or to prevent transition to a configuration of opposite chirality (a mirror image).