Optimal spline cutoffs for Coulomb and van der Waals interactions

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Traditional spline cutoffs of the long-ranged Coulomb interaction gives large errors in the forces which lead to seriously distorted structures. These errors can be drastically reduced (by a factor of 7) by optimally adjusting the cutoffs parameters. Applying to a 453-atom dendrimer, the visibly distorted structure is improved substantially (the rms coordinate deviation is reduced from 1.15 to 0.55 Å).

1. Introduction

In molecular dynamics and molecular mechanics calculations of proteins, polymers, and ceramics, the calculation costs are dominated by the non-bonding long-range interactions

$$V=\sum_{i>j}\frac{q_i q_j}{R_{ij}^p}, \tag{1}$$

where $p=1$ is the Coulomb interaction; $p=2$ is the screened Coulomb interaction which often replaces the standard Coulomb interaction to account for solvent effects in biomolecules; $p=6$ is the van der Waals interaction. Since the number of such interactions is of the order N^2 (N being the number of atoms) a common approach has been to cut off the interaction at a fixed distance R_{out}. Using a list of non-bonding interactions (updated only occasionally) the overall scale of the calculations is order N for a fixed cutoff, making calculations of large molecules (a few thousand atoms) practical.

To prevent [1,2] discontinuities in energy and forces, the potential $V(R)$ is replaced by $V(R)S(R^2)$ where the function $S(R)$ changes smoothly from 1 at $R=R_{in}$ to zero at $R=R_{out}$. The most common smoothing function (e.g. AMBER [1], CHARMM [2]) is a cubic spline function,

$$S(R^2)=\frac{(R_{out}^2-R^2)^2(R_{out}^2+2R^2-3R_{in}^2)}{(R_{out}^2-R_{in}^2)^3}, \tag{2}$$

where the commonly used cutoff distance is

$$R_{out}=10.5\ \text{Å} \tag{3a}$$

and the smoothing region of

$$\Delta\equiv R_{out}-R_{in}=1\ \text{Å}, \tag{3b}$$

as in CHARMM [1], or $R_{out}=9$ Å (AMBER [2]) with the same smoothing region.

However, in analyzing the accuracy of this method, we find that use of such cutoff leads to very substantial errors in forces. As a prototype to illustrate the errors we consider the non-bonding Coulomb interaction on a 4th generation β-alanine starburst dendrimer [3] which has 453 atoms and a size of 50 Å wide. Using the traditional cutoffs (3) leads to rms forces errors of 29% (13 kcal/mol Å) and a total energy error of 0.33% (38 kcal/mol) (for a starting structure built with standard angles and distances). Such large errors in the forces are significant since the point of most simulations is to use forces to *predict* geometries or dynamics. To appreciate the significance of such errors we compare in fig. 1 the structures obtained with exact functions (no cut-

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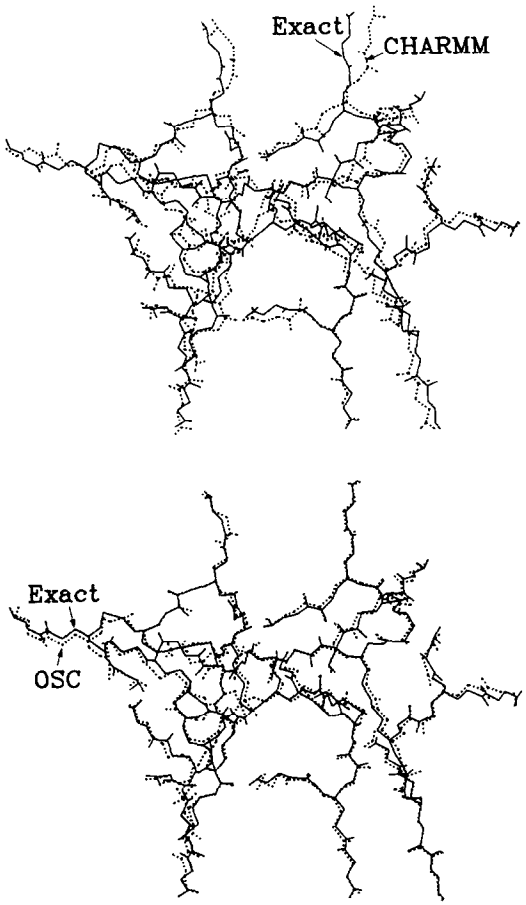

Fig. 1. Dendrimer structures obtained (upper) using traditional (CHARMM) cutoff parameters $(R_{in}, R_{out}) = (9.5, 10.5)$ and (lower) using optimal spline cutoffs (4.5, 10.5). Both structures are obtained starting with the exact structure (with no cutoffs). The traditional cutoffs lead to a structure with an rms coordinate error of 1.15 Å, while the OSC cutoffs lead to an error of 0.55 Å.

offs) to the traditional cutoffs. The traditional cutoffs (eq. (3)) lead to a visibly distorted structure, with an rms coordinate deviation of 1.15 Å. This is unacceptably large and suggests that other properties might have even more serious errors.

It is attempting to attribute these large errors to the cutoff of the long-range tails of the interaction, which is generally costly to compute. But when we substantially increase the cutoff distance to $R_{out} = 25$ Å (the computational effort increases by a factor of 14), the rms coordinate deviation decreases only slightly (to 0.87 Å) which is still too large. In fact, we find that the errors decrease very slowly ($\propto R_{out}^{-1/2}$) as the cutoff increases, while the computational effort increases very fast ($\propto R_{out}^3$)! On the other hand, however, we find that suitable adjustment of the smooth region could dramatically reduce these errors. In particular, the optical choice of

$$R_{in}^{OSC} = 0.4289\, R_{out} \approx \tfrac{3}{7} R_{out}\,, \tag{4a}$$

i.e. a much wider smoothing range, reduce the force errors by a factor of 7 for Coulomb interactions. Using this R_{in}^{OSC} in minimizing the 453-atom dendrimer structure, the coordinate deviation is reduced very substantially (see fig. 1). The rms coordinate error is reduced from 1.15 to 0.55 Å for the standard $R_{out} = 10.5$ Å. For a larger cutoff $R_{out} = 25$ Å, the rms error is reduced from 0.87 to 0.24 Å.

2. Optimal spline cutoffs

We have systematically analyzed the cutoff method. The key point we found is that the seemingly smooth function applied to the potential energy in fact introduces a peak in the force which leads to large errors. Let us focus on the Coulomb interaction. Since the energy is $V(R) = (1/R)S(R^2)$, the force has a form of

$$F(R) = -\frac{\mathrm{d}V(R)}{\mathrm{d}R}\hat{e}_R = \frac{S(R^2)}{R^2}\hat{e}_R - 2\frac{\mathrm{d}S(R^2)}{\mathrm{d}R^2}\hat{e}_R\,, \tag{5}$$

where $\hat{e}_R$ is a unit vector linking the two charges (assumed to be unit here). As indicated in fig. 2 the derivative of the smooth function (the second term) has a large peak for the traditional cutoffs ($\Delta = 1$ Å), which leads to a large error in the force. Comparing to the error arising from the truncation of the long range interaction tails (in first term), this error is more pronounced and we analyze this error in this paper.

By a statistical argument, we estimate the force error due to this peak to be

$$(\delta F)_{rms} \propto \frac{(3R_{out}^2\Delta - 3R_{out}\Delta^2 + \Delta^3)^{1/4}}{(R_{out} - \frac{1}{2}\Delta)\Delta}\,, \tag{6}$$

for small Δ. Consider an atom at origin and its interactions with all other atoms. The atoms inside the

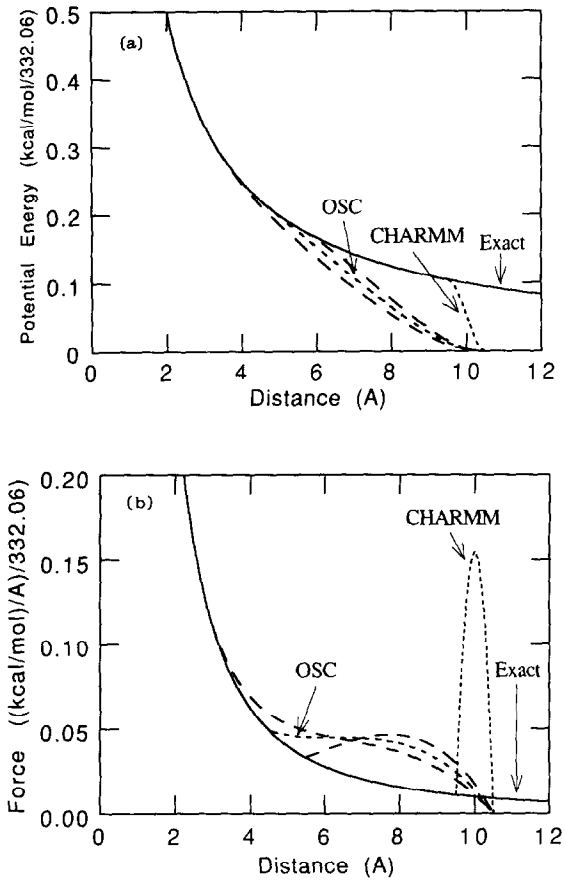

Fig. 2. Effect of spline smoothing on (a) the potential energy and (b) the force. The traditional (CHARMM) cutoff parameters are $(R_{in}, R_{out}) = (9.5, 10.5)$ while OSC uses (4.5, 10.5). The two unmarked curves use cutoff parameters of (3, 10.5) and (5.5, 10.5), showing the sensitivity to the OSC choice.

sphere of $R \leqslant R_{in}$ contribute only to the first term in eq. (5). Atoms outside the sphere of $R = R_{out}$ are ignored in the cutoff method. Atoms inside the spherical shell (R_{in}, R_{out}) contribute to the second term which incorrectly gives an average force $= \frac{1}{2}$(height of the peak) instead of the correct $1/R^2$. (In this estimate, all charges are assumed to be ± 1.) Since the peak height is $1.5/(R_{out} - \frac{1}{2}\Delta)\Delta$, the force error is $\delta F_{rms} \propto N_{eff}/(R_{out} - \frac{1}{2}\Delta)\Delta$, where N_{eff} is the effective number of contributions. In adding the contributions to the central atom, we have to sum over positive and negative charges in the shell. Should the positive charges distribute exactly as those negative charges, they would cancel out exactly and N_{eff} would be zero. But in reality the positive and negative charges fluctuate, and by the law of large numbers [4], the rms value is expected to be $N_{eff} \propto N_{tot}^{1/2}$ where $N_{tot} = (4\pi\rho/3)(R_{out}^3 - R_{in}^3)$ is the total number of atoms in the shell (ρ is density). Furthermore, force is a vector. Consider the x direction. Should the positive charges distribute exactly symmetrically in $+x$, $-x$ directions, F_x would be zero by cancellation. But in reality, this cancellation is not exact and the rms net value would be $\propto$(number of charges)$^{1/2}$. The same applies to negative charges, and to y, z directions. Hence, these direction fluctuations further reduce N_{eff} to $N_{eff} \propto N_{tot}^{1/4}$. This gives our estimate (6).

Traditional choices use a narrow smoothing region of $\Delta \approx 1$ Å. In this case, eq. (6) reduces to

$$\delta F_{rms} \propto \Delta^{-3/4} R_{out}^{-1/2} . \tag{7}$$

Thus for a given Δ, the errors decrease according to $R_{out}^{-1/2}$ which agrees with direct calculation (see fig. 3). Consequently, to reduce the force errors by a factor of two, one needs to increase R_{out} by a factor of 4. Since the computer time grows as R_{out}^3, this increases the computer time by a factor of 64!

On the other hand, for a given R_{out}, doubling Δ reduces the error by about a factor of 1.7. Clearly increasing Δ can increase the accuracy, but which value is the best choice? As evident in fig. 2b, the peak in the force curve flattens as Δ increases (R_{in} de-

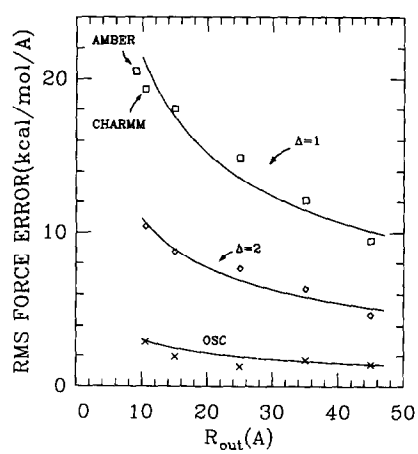

Fig. 3. rms force errors calculated for the 7th generation dendrimer (3813 atoms with a diameter of 79 Å). The lines for $\Delta = 1$ Å and $\Delta = 2$ Å are based on eq. (7). The OSC choice at each R_{out} is determined from eq. (4a). The OSC errors are about seven times smaller than those for traditional cutoffs ($\Delta = 1$ Å) at all R_{out}. The curve through the OSC data is proportional to $R_{out}^{-1/2}$.

creases), and the force error (6) becomes smaller. The actual rms errors are plotted in fig. 4 for two cases, $R_{out}=10.5$ Å and $R_{out}=25$ Å. For small Δ, the force error decreases very quickly as Δ is increased, as expected from (6); the improvement becomes insignificant for $R_{in}<0.5R_{out}$. Although this example gives the smallest error for $R_{in}\approx 0$, general considerations [1,2] suggest that $R_{in}\approx 0$ leads to significant changes in short-range correlations and should be excluded.

The above investigations clearly indicate the dominant effects of the peak in the force function. Thus we further analyze the force function (see fig. 2b) and derive optimal cutoff parameters. The correct forces decrease monotonically with distance ($dF_r/dr\leqslant 0$), whereas the modified forces have $dF_r/dr>0$ in some region when R_{in} is close to R_{out}. We believe that such non-monotonic force functions would lead to unphysical behavior and should be excluded. On the other hand, R_{in} should not be small so that the short-range interactions are not affected. Our choice is to make R_{in} smaller gradually until the modified force function eq. (5) becomes monotonic. This leads to the optimal choice in eq. (4a) for Coulomb interactions. As indicated in fig. 2b, this choice eliminates the hump in the cases of $R_{in}>R_{in}^{OSC}$, while not affecting the short-range forces. The rms force errors are reduced dramatically, by a factor of 7 for the conventional cutoff $R_{out}=10.5$ Å (see table 1). The energy errors remain about the same.

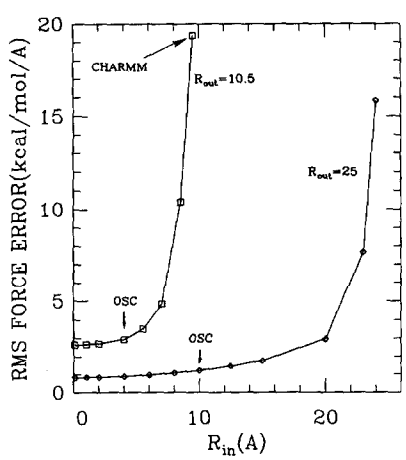

Fig. 4. The dependence of rms force error (for the 7th generation dendrimer) on R_{in} for fixed cutoffs at $R_{out}=10.5$ and 25 Å.

For the van der Waals interaction, C_{ij}/R_{ij}^6, the same criteria lead to

$$R_{in}^{OSC}=(1+\sqrt{4/7})^{-1/2}R_{out}\approx\tfrac{3}{4}R_{out}\,, \tag{4b}$$

which is larger than for the Coulombic case, as expected. For the screened Coulomb interaction z_iz_j/R_{ij}^2 widely used to mimic solvent effects in modeling of biomolecules, the optimum choice is

$$R_{in}^{OSC}=(1/\sqrt{3})R_{out}\approx\tfrac{4}{7}R_{out}\,, \tag{4c}$$

a value between the pure Coulomb (3/7) and the van der Waals (3/4) cases.

In most systems both Coulomb and dispersion potentials are present, and it is often convenient to use the same smoothing function for all non-bonding terms,

$$V_{\text{non-bond}}=\sum_{i<j}\left(\frac{q_iq_j}{R_{ij}}+\frac{B_{ij}}{R_{ij}^{12}}-\frac{C_{ij}}{R_{ij}^6}\right)S(R_{ij}^2)\,.$$

In such situations, the optimal choice should be dictated by the Coulombic part, (4a) or (4c), because the peak in the Coulomb force is much more pronounced and the Coulomb interaction is usually more important.

Applying the optimal cutoff has a dramatic effect. In fig. 1 we show the optimum structure for the 4th generation dendrimer for both traditional and optimal cutoffs (comparing with the reference structure obtained using no cutoffs). The traditional cutoffs (R_{in}, R_{out}) = (9.5 Å, 10.5 Å) lead to a visibly distorted structure, with an rms deviation 1.15 Å (over all atoms in the structure). Using the optimal cutoff (4.5 Å, 10.5 Å), the structure improves very substantially, with an rms deviation of 0.55 Å (see table 1). The alternative of simply increasing the cutoff to 25 Å (while fixing $\Delta=1$ Å) still leads to an unacceptability large rms deviation of 0.87 Å, even though the computation time is increased $(25/10.5)^3\approx 14$ times. However using the optimal (10.7 Å, 25 Å), the rms coordinate deviation reduces to 0.235 Å! Since high resolution X-ray diffraction can obtain accuracies of 0.5 Å, the optimal cutoff should be used to obtain structures for comparison to experiment.

Table 1
Errors in energies, forces and structures for various choices of cutoffs for the fourth generation (453-atom) β-alanine starburst dendrimer. These calculations use the AMBER force field for the charges and valence interactions. The error in energy and forces is for the starting structure using standard bonds and angles. The coordinate error is after conjugate gradient minimization to an rms force error of 0.1 kcal/mol Å

R_{out} (Å)	R_{in} (Å)	Choice	Energy error (kcal/mol)	rms force error (kcal/mol Å)	rms coordinate error (Å)
9	8	AMBER	−49.8	15.2	1.33
10.5	9.5	CHARMM	−38.4	13.2	1.15
10.5	4.5	OSC	−2.3	1.76	0.55
25	24	-	43.6	9.14	0.87
25	10.7	OSC	−32.3	0.80	0.24

3. Discussions

Our study suggests that a large part of the error in the spline cutoff method is due to the peak in the derivative of the spline function, rather than due to the neglected long range tails of the interaction.

Both general arguments and the calculations as exemplified in fig. 3, indicate that as the cutoff distance increases, errors decrease very slowly ($\propto R_{out}^{-1/2}$ for Coulomb forces), in contrast to simple intuitions.

The large smoothing range in the optimal spline cutoff may contradict the general belief that the smoothing range should be small. But it works quite well. The reason is due to the very slow decrease in the error ($\sim R_{out}^{-1/2}$). A cutoff $R_{out}=5$ Å differs very little from a cutoff $R_{out}=10$ Å, as far as errors are concerned. But widening the smoothing range reduces dramatically the peak in the derivative of the spline function which in turn leads to a large reduction in force errors. Therefore, increasing $R_{out}-R_{in}$ is much more important than increasing the cutoff distance R_{out}.

Since the spline cutoff method is widely used for molecular simulations, these optimal spline cutoffs should allow the quality of the simulations to be improved significantly at no increase in computational cost.

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