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Particle mesh Ewald: An $N \cdot \log(N)$ method for Ewald sums in large systems

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An $N \cdot \log(N)$ method for evaluating electrostatic energies and forces of large periodic systems is presented. The method is based on interpolation of the reciprocal space Ewald sums and evaluation of the resulting convolutions using fast Fourier transforms. Timings and accuracies are presented for three large crystalline ionic systems.

INTRODUCTION

We consider a lattice Λ defined by elementary translation vectors \mathbf{a}_1 , \mathbf{a}_2 , and \mathbf{a}_3 with Euclidean lengths a_1 , a_2 , and a_3 , respectively. The Cartesian components of the k th lattice vector, \mathbf{a}_k , are denoted a_{k_l} ($l=1,2,3$). The conjugate reciprocal lattice Λ^* is defined by elementary translations \mathbf{a}_1^* , \mathbf{a}_2^* , and \mathbf{a}_3^* , with Euclidean lengths a_1^* , a_2^* , and a_3^* , and Cartesian components $a_{k_l}^*$ ($k,l=1,2,3$). These reciprocal translations satisfy $\mathbf{a}_k^* \cdot \mathbf{a}_l = \delta_{kl}$ ($k,l=1,2,3$). The unit cell U of the lattice Λ consists of all points \mathbf{r} having fractional coordinates (f_1, f_2, f_3) with $-\frac{1}{2} < f_k < \frac{1}{2}$, for $k=1,2,3$ (where $f_k = \mathbf{a}_k^* \cdot \mathbf{r}$).

We define the functions $\Phi_{\text{dir}}(\mathbf{r};\beta)$ and $\Phi_{\text{rec}}(\mathbf{r};\beta)$, where \mathbf{r} is a point in U and β is a positive number, by

$$\Phi_{\text{dir}}(\mathbf{r};\beta) = \sum_{\mathbf{n}} \frac{\text{erfc}(\beta|\mathbf{r}+\mathbf{n}|)}{|\mathbf{r}+\mathbf{n}|}$$

and

$$\Phi_{\text{rec}}(\mathbf{r};\beta) = \frac{1}{\pi V} \sum_{\mathbf{m} \neq 0} \frac{\exp(-\pi^2 \mathbf{m}^2 / \beta^2)}{\mathbf{m}^2} \exp(2\pi i \mathbf{m} \cdot \mathbf{r}), \quad (1)$$

where $\text{erfc}(x)$ is the complementary error function, $V = \mathbf{a}_1 \cdot \mathbf{a}_2 \times \mathbf{a}_3$ is the volume of the unit cell U , and \mathbf{n} and \mathbf{m} are given by $\mathbf{n} = n_1 \mathbf{a}_1 + n_2 \mathbf{a}_2 + n_3 \mathbf{a}_3$, and $\mathbf{m} = m_1 \mathbf{a}_1^* + m_2 \mathbf{a}_2^* + m_3 \mathbf{a}_3^*$, for integers n_k and m_k ($k=1,2,3$). The effect of β on the Ewald pair potential, $\psi(\mathbf{r};\beta)$, defined by $\psi(\mathbf{r}) = \Phi_{\text{dir}}(\mathbf{r};\beta) + \Phi_{\text{rec}}(\mathbf{r};\beta)$, is that of an additive constant. Hence, for a neutral system, the total electrostatic energy (and its derivatives) are invariant to β .

The infinite series defining Φ_{dir} and Φ_{rec} are both rapidly convergent. Their rates of convergence are controlled by adjusting the value of β . If β is chosen so that only the minimum image terms in the direct space sum $\Phi_{\text{dir}}(\mathbf{r};\beta)$ are retained, the total electrostatic energy of a neutral unit cell U , containing N point charges q_1, q_2, \dots, q_N , located at positions $\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N$, is given by¹⁻³

$$E = \sum_{i=1}^N \sum_{j=i+1}^N q_i q_j \frac{\text{erfc}(\beta r_{ij})}{r_{ij}} - \frac{\beta}{\sqrt{\pi}} \sum_{i=1}^N q_i^2 + \frac{1}{2} \sum_{i=1}^N \sum_{j=1}^N q_i q_j \Phi_{\text{rec}}(\mathbf{r}_j - \mathbf{r}_i; \beta) + J(\mathbf{D}), \quad (2)$$

where r_{ij} is the minimum image distance. De Leeuw *et al.*¹ derived the fourth term $J(\mathbf{D})$ in Eq. (2), which depends quadratically on the dipole moment \mathbf{D} of the unit cell, as well as the macroscopic boundary conditions of the crystal and the external dielectric constant.

Choosing β as above makes evaluation of the electrostatic energy an order N^2 computational problem. Adjusting β to optimize computational effort results in an order $N^{3/2}$ algorithm.⁴ Although conventional Ewald summation is widely used for simulations of small periodic systems, the computational cost becomes prohibitive for large ($N > 10^4$) macromolecular simulations. Alternative techniques for improving the evaluation of long range electrostatic forces include expansion of the Ewald pair potential in cubic polynomials,⁵ table lookup of the pair potential,⁶ use of Wigner potentials,⁷ multiple time step ("twin range") methods,⁸ particle-mesh techniques,⁹ and efficient Taylor and/or multipole expansions.¹⁰⁻¹⁵

The particle-mesh Ewald (PME) method presented here involves choosing β sufficiently large that atom pairs for which r_{ij} exceeds a specified cutoff (e.g., 9 Å) are negligible in the direct space sum in Eq. (2) which reduces this term to order N . The reciprocal space sum in Eq. (2) is then approximated by a multidimensional piecewise-interpolation approach inspired by the particle-mesh method of Hockney and Eastwood.⁹ The approximate reciprocal energy and forces are expressed as convolutions and can thus be evaluated quickly using fast Fourier transforms (FFTs). The resulting algorithm is of order $N \ln(N)$, is easily programmed, and is shown below to be efficient and accurate for macromolecular systems.

METHOD

If $\Phi_{\text{rec}}(\mathbf{r};\beta)$ is expressed in fractional coordinates $\{f_i\}$ we have

$$\Phi_{\text{rec}}(f_1, f_2, f_3; \beta) = \frac{1}{\pi V} \sum_{\mathbf{m} \neq 0} \frac{\exp(-\pi^2 \mathbf{m}^2 / \beta^2)}{\mathbf{m}^2} \times \exp[2\pi i(m_1 f_1 + m_2 f_2 + m_3 f_3)]. \quad (3)$$

Given positive integers K_1 , K_2 , and K_3 , we compute Φ_{rec} as well as its (Cartesian) gradient on the grid of fractional coordinates $(l_1/K_1, l_2/K_2, l_3/K_3)$, for $l_k = 1, \dots, K_k$,

$k=1,2,3$, and store these quantities into arrays at the beginning of the simulation. Given a pair of atoms i and j , with fractional coordinates f_{i_k} and f_{j_k} , $k=1,2,3$, the in-

terpolation approximation (order p) to the reciprocal space pair potential, $\hat{\Phi}_{\text{rec},p}$, at each point is given in terms of the precomputed array values of Φ_{rec} ,

$$\hat{\Phi}_{\text{rec},p}(f_{j_1}-f_{i_1}, f_{j_2}-f_{i_2}, f_{j_3}-f_{i_3}; \beta) = \sum_{k_1, k_2, k_3} \theta_{p, K_1}(f_{i_1}, k_1) \theta_{p, K_2}(f_{i_2}, k_2) \theta_{p, K_3}(f_{i_3}, k_3) \cdot \sum_{l_1, l_2, l_3} \theta_{p, K_1}(f_{j_1}, l_1) \theta_{p, K_2}(f_{j_2}, l_2) \theta_{p, K_3}(f_{j_3}, l_3) \cdot \Phi_{\text{rec}}\left(\frac{l_1-k_1}{K_1}, \frac{l_2-k_2}{K_2}, \frac{l_3-k_3}{K_3}\right), \quad (4)$$

where the functions $\theta_{p,K}$ are obtained from the barycentric form of the weights used in $(2p-1)$ th order Lagrangian interpolation using the grid of points (k/K) , $k \in \mathcal{Z}$.¹⁶ More specifically, for real argument x , let $[x]$ denote the largest integer less than or equal to x , and define the integer function $k_{p,K}(x)$ by $k_{p,K}(x) = [Kx] - p + 1$. Next define $\phi_{p,K}(x, k)$ by

$$\phi_{p,K}(x, k) = \frac{(-1)^k \binom{2p-1}{k} \frac{1}{\left(x - \frac{k}{K}\right)}}{\sum_{l=0}^{2p-1} (-1)^l \binom{2p-1}{l} \frac{1}{\left(x - \frac{l}{K}\right)}} \quad \text{for } 0 \leq k \leq 2p-1$$

$$= 0 \quad \text{otherwise,} \quad (5)$$

and finally let $\theta_{p,K}(x, k) = \phi_{p,K}[x - k_{p,K}(x), k - k_{p,K}(x)]$. Note that $\theta_{p,K}(x, k)$ is nonzero for $2p$ values of k , and that the sum of $\theta_{p,K}(x, k)$ over all k is unity. Since $\theta_{p,K}(k/K, k) = 1$ and $\theta_{p,K}(l/K, k) = 0$ for $l \neq k$, we see that $\theta_{p,K}(x, k)$ are continuous in x . Note also that x is always in the central grid interval, with respect to the weights, so that we avoid the ill-conditioning associated with high order polynomial interpolation. The approximate gradient is obtained by replacing Φ_{rec} in Eq. (4) by its gradient, obtained by term-by-term differentiation, at each grid point.

Defining Q at the grid points by

$$Q\left(\frac{l_1}{K_1}, \frac{l_2}{K_2}, \frac{l_3}{K_3}\right) = \sum_{j=1}^N q_j \theta_{p, K_1}(f_{j_1}, l_1) \theta_{p, K_2}(f_{j_2}, l_2) \times \theta_{p, K_3}(f_{j_3}, l_3), \quad (6)$$

the expression for the approximate reciprocal sum energy $\hat{E}_{\text{rec},p}(i)$ at atom i due to the atoms of the unit cell U is

$$\hat{E}_{\text{rec},p}(i) = \frac{1}{2} \sum_{k_1, k_2, k_3} q_i \theta_{p, K_1}(f_{i_1}, k_1) \theta_{p, K_2}(f_{i_2}, k_2) \times \theta_{p, K_3}(f_{i_3}, k_3).$$

$$\sum_{l_1, l_2, l_3} Q\left(\frac{l_1}{K_1}, \frac{l_2}{K_2}, \frac{l_3}{K_3}\right) \Phi_{\text{rec}}\left(\frac{l_1-k_1}{K_1}, \frac{l_2-k_2}{K_2}, \frac{l_3-k_3}{K_3}\right) = \frac{1}{2} \sum_{k_1, k_2, k_3} q_i \theta_{p, K_1}(f_{i_1}, k_1) \theta_{p, K_2}(f_{i_2}, k_2) \theta_{p, K_3}(f_{i_3}, k_3) \cdot \Phi_{\text{rec}} * Q\left(\frac{k_1}{K_1}, \frac{k_2}{K_2}, \frac{k_3}{K_3}\right), \quad (7)$$

where $\Phi_{\text{rec}} * Q$ denotes the discrete convolution operator, and we have used the fact that $\Phi_{\text{rec}}(\mathbf{r}; \beta) = \Phi_{\text{rec}}(-\mathbf{r}; \beta)$. Since $\theta_{p,K}(x, k)$ is continuous in x , the approximate energies and forces will be continuous with respect to particle position, which is not true of the cell multipole methods.¹⁰⁻¹⁵ We can evaluate $\Phi_{\text{rec}} * Q$ using the fast Fourier transform in order $K_1 K_2 K_3 \log(K_1 K_2 K_3)$ steps, whereas evaluation of Q and $\hat{E}_{\text{rec},p}(i)$, $i=1, \dots, N$ can be achieved in order $(2p)^2 \cdot N$ steps. Similar results hold for evaluation of the gradient. In practice, we pack Φ_{rec} and its three gradient components at the grid points into two complex arrays and precompute their Fourier transform (FT) once at the start of the simulation. At each subsequent step we compute Q as a complex array, transform it, multiply the transformed components by the precomputed complex arrays at each grid point, and then back transform the resulting pair of complex arrays.

An upper bound for the absolute error $|\hat{\Phi}_{\text{rec},p} - \Phi_{\text{rec}}|$ can be estimated as follows. Given integers m , and $K > 0$, from standard error estimates on Lagrangian interpolation¹⁶ we have for all x

$$|\exp(2\pi i m x) - \sum_{k \in \mathcal{Z}} \exp\left(2\pi i m \frac{k}{K}\right) \theta_{p,K}(x, k)| < 2 \binom{2p}{p} \left(\frac{m}{4K}\right)^{2p}. \quad (8)$$

From Eqs. (4) and (8) we see that, pointwise

$$|\hat{\Phi}_{\text{rec},p} - \Phi_{\text{rec},p}| < 4 \binom{2p}{p} \frac{1}{\pi V} \sum_{m \neq 0} \frac{\exp(-\pi^2 m^2 / \beta^2)}{m^2} \times \left[\left(\frac{m_1}{4K_1}\right)^{2p} + \left(\frac{m_2}{4K_2}\right)^{2p} + \left(\frac{m_3}{4K_3}\right)^{2p} \right]. \quad (9)$$

The right hand side of Eq. (9) can be estimated by replacing the sum by an integral. We can change variables

TABLE I. The relative potential error (rmsE), relative force error (rmsf), and maximum relative force error (maxerrf) are: $\text{rmsE} = [(E - \hat{E})^2 / E^2]^{1/2}$, $\text{rmsf} = [\sum_i^N (\mathbf{f}_i - \hat{\mathbf{f}}_i)^2 / \sum_i^N \mathbf{f}_i^2]^{1/2}$, and $\text{maxerrf} = \max\{[(\mathbf{f}_i - \hat{\mathbf{f}}_i)^2 / \mathbf{f}_i^2]^{1/2}; 1 < i < N\}$; where E is the total electrostatic energy and \mathbf{f}_i is the force vector at atom i , evaluated using the exact Ewald pair potential for all atom pairs. The “ $\hat{}$ ” symbol indicates the approximate values evaluated with the PME method using a 9 Å atom-based list for the direct space contribution. The percent overhead (% overhead) is: $\text{time}^{\text{PME}} / \text{time}^{\text{Coulomb}} \times 100\%$; where time^{PME} is the time for evaluation of the total nonbond potential energy and forces using the PME method for the electrostatics, and $\text{time}^{\text{Coulomb}}$ is the time (2.28 s for B-DNA) required for evaluation of the total nonbond energy and forces using conventional Coulombic interactions.

Order p		Approximate grid size (Å)/Dimensions (K_1, K_2, K_3)		
		1.0 (24,40,64)	0.75 (32,54,96)	0.5 (48,81,128)
1	rmsE	4.9×10^{-3}	3.1×10^{-3}	2.0×10^{-3}
	rmsf	2.9×10^{-2}	1.4×10^{-2}	7.5×10^{-3}
	maxerrf	0.50	0.36	0.17
	% overhead	16.2%	21.5%	39.9%
2	rmsE	1.4×10^{-3}	4.3×10^{-4}	1.1×10^{-4}
	rmsf	4.0×10^{-3}	1.1×10^{-3}	2.6×10^{-4}
	maxerrf	0.13	2.8×10^{-2}	6.1×10^{-3}
	% overhead	21.5%	26.8%	45.2%
3	rmsE	5.0×10^{-4}	9.1×10^{-5}	1.1×10^{-5}
	rmsf	1.0×10^{-3}	1.6×10^{-4}	1.9×10^{-5}
	maxerrf	4.3×10^{-2}	3.4×10^{-3}	4.0×10^{-4}
	% overhead	35.5%	39.9%	58.3%
4	rmsE	2.2×10^{-4}	2.5×10^{-5}	1.7×10^{-6}
	rmsf	3.7×10^{-4}	3.7×10^{-5}	5.7×10^{-6}
	maxerrf	1.6×10^{-2}	7.4×10^{-4}	1.5×10^{-4}
	% overhead	62.2%	64.9%	83.8%

in the integral by $x_k = a_{1k}^* m_1 + a_{2k}^* m_2 + a_{3k}^* m_3$, and $m_k = a_{k1} x_1 + a_{k2} x_2 + a_{k3} x_3$, for $k=1,2,3$. If we then transform to spherical coordinates, and apply the Cauchy-Schwarz inequality to the quantities m_k , $k=1,2,3$, we see, using standard results on the moments of Gaussian distributions,¹⁷ that the right hand side of Eq. (9) is bounded from above by

$$8 \binom{2p}{p} \frac{(2p)!}{p!} \frac{\beta}{\sqrt{\pi}} \left(\frac{\beta}{8\pi} \right)^{2p} \left[\left(\frac{a_1}{K_1} \right)^{2p} + \left(\frac{a_2}{K_2} \right)^{2p} + \left(\frac{a_3}{K_3} \right)^{2p} \right]. \quad (10)$$

A similar result can be obtained for the gradient. The error in the interpolation can be made arbitrarily small by fixing a_1/K_1 , a_2/K_2 , and a_3/K_3 to be less than one, and then choosing p sufficiently large. Thus, the quantity $K_1 K_2 K_3$ is of order the system size $a_1 a_2 a_3$ and hence of order N , for any desired tolerance, and so the proposed algorithm is of order $N \log(N)$.

RESULTS

The PME method was implemented by modifying the AMBER3.0 (Rev. A) molecular dynamics code in the following way. The direct space pair potential, Φ_{dir} , was computed along with the van der Waals and H-bond terms from an atom-based nonbond list. The $\text{erfc}(x)$ function and its derivative were obtained by table look up (relative error $\leq 1.0 \times 10^{-8}$) for increased efficiency. The approximate reciprocal space pair potential $\hat{\Phi}_{\text{rec}}$ was evaluated as described above in a separate routine. An additional cor-

rection was needed to account for exclusion of nearest images of masked atom pairs (bonded pairs, etc.). All tests were run as single processor jobs on the Cray YMP at the Frederick Cancer Research and Development Center.

The accuracy and computational efficiency of the PME method were tested on several macromolecular crystals. Unit cells were constructed from the space groups using the crystallographic coordinates for the heavy atom positions, as in previous work.^{18,19} Point charges were assigned using the AMBER force field.²⁰ Electrostatic energies and forces for each atom are compared to the corresponding values calculated using the exact Ewald pair potential (relative accuracy $\leq 1 \times 10^{-7}$).

Table I shows the results for an ionic B-DNA crystal.²¹ Results are given for grid densities $(a_1/K_1 \times a_2/K_2 \times a_3/K_3)^{1/3}$ of approximately 1.0, 0.75, and 0.5 Å, and interpolation order $p=1,2,3,4$. The computational cost of the PME method is compared to that of normal evaluation of nonbond interactions using a 9 Å atom-based Verlet list on a single processor Cray YMP. The overhead above normal nonbond interactions ranges from approximately 16% to 84% corresponding to root mean square (rms) relative force errors of 2.9×10^{-2} and 5.7×10^{-6} , respectively. We conclude that reasonable relative accuracy (about 2×10^{-4} rms force error) can be obtained with approximately a 40% overhead, by using triquintic interpolation ($p=3$) on a 0.75 Å grid. Similar accuracies and computational costs are obtained for large protein crystals^{22,23} using comparable grid densities and interpolation orders (Table II). Note

TABLE II. Accuracy and timings for several crystal unit cells. Triquintic interpolation ($p=3$) was used for each system. In each case β was chosen to be 0.386.

	B-DNA (Ref. 21)	HIV-1 PR (Ref. 22)	$p21$ (Ref. 23)
Space group	$P2_12_12_1$	$P4_12_12$	$P3_221$
a, b, c (Å)	24.87, 40.39, 66.20	50.24, 50.24, 106.56	40.3, 40.3, 162.2
α, β, γ (°)	90, 90, 90	90, 90, 90	90, 90, 120
No. of atoms	7938	29 661	25 797
Approximate grid size	0.75 Å	0.84 Å	0.80 Å
Grid dimensions (K_1, K_2, K_3)	(32, 54, 96)	(64, 64, 128)	(48, 48, 192)
rmsE	9.1×10^{-5}	3.6×10^{-5}	4.9×10^{-5}
rmsf	1.6×10^{-4}	1.6×10^{-4}	2.3×10^{-4}
maxerrf	3.4×10^{-3}	1.2×10^{-2}	1.4×10^{-2}
time ^{PME}	3.19 s	10.76 s	9.46 s
% overhead	39.9%	39.0%	43.3%

the PME method is completely general to nonorthogonal unit cells.

Traditional particle-mesh techniques have been criticized as not being able to attain high accuracy efficiently, especially for nonuniform particle distributions.¹¹ Our results indicate that high precision (rms relative force error $< 1.0 \times 10^{-5}$) is easily obtained for macromolecular systems by using higher order interpolation with only a modest increase in computational time. Although the PME method has increased memory requirements over conventional nonbond list-based methods, the cost of memory appears to be rapidly decreasing, and hence may not be an issue in the future.

The PME method offers several advantages as a method for the treatment of long-range forces in macromolecular systems. These include

(1) *High accuracy*: High accuracy ($\approx 5 \times 10^{-6}$ relative force) can be obtained with relatively little increase in computational effort.

(2) *Easy of implementation*: The PME method can be efficiently implemented into conventional MD algorithms such as AMBER which use a Verlet list.

(3) *Continuity*: The PME pair potential and its derivatives are continuous functions of position, regardless of the accuracy required, and thus avoid problems involved with integration of discontinuous functions.

(4) *Efficiency*: The PME method is fast. For large macromolecular systems, the PME method requires only

about a 40% overhead over conventional truncated list-based methods to obtain relative force accuracies of $\approx 2 \times 10^{-4}$.

The FORTRAN subroutines for performing the PME approximate energies and forces are available upon request from the authors.

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