Optimal Physical Multipoles

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Abstract

Point multipole expansions are widely used to gain physical insight into complex distributions of charges and to reduce the cost of computing interactions between such distributions. However, practical applications that typically retain only a few leading terms may suffer from unacceptable loss of accuracy in the near-field. We propose an alternative approach for approximating electrostatic charge distributions, Optimal Physical Multipoles (OPMs), which optimally represent the original charge distribution with a set of point charges. By construction, approximation of electrostatic potential based on OPMs retains many of the useful properties of the corresponding point multipole expansion, including the same asymptotic behavior of the approximate potential for a given multipole order. At the same time, OPMs can be significantly more accurate in the near field: up to 5 times more accurate for some of the charge distributions tested here which are relevant to biomolecular modeling. Unlike point multipoles, for point charge distributions the OPM always converges to the original point charge distribution at finite order. Furthermore, OPMs may be more computationally efficient and easier to implement into existing molecular simulations software packages than approximation schemes based on point multipoles. In addition to providing a general framework for computing OPMs to any order, closed-form expressions for the lowest order OPMs (monopole and dipole) are derived. Thus, for some practi-
cal applications Optimal Physical Multipoles may represent a preferable alternative to point multipoles.

1 Introduction

Point multipole expansions are widely used to gain physical insight by providing a simplified expression for a complex distribution of sources of potential fields, such as electrostatic potential due to a charge distribution. Point multipoles provide a means of decoupling the underlying features of a source distribution from the observation point. Thus, one can obtain physically meaningful insights into the macroscopic properties of the distribution, such as the familiar dipole moment.

In addition to having theoretical utility, the point multipole expansion has been used to simplify practical calculations. For example, algorithms such as the fast multipole method [11], use point multipoles to reduce the computational complexity of calculating pairwise interactions between large charge distributions. Let $R_0$ be the distance of the furthest charge in the distribution from the expansion center. Since each successive term in the multipole expansion decays more rapidly with distance than the previous term, at large distances $R \gg R_0$ the series converges quickly and so these methods are able to obtain reasonably accurate results by keeping only the lowest order terms. However, at distances not much larger than $R_0$, the accuracy of the approximation deteriorates quickly. Since, in practice, the potential often needs to be calculated in regions where the assumption $R \gg R_0$ does not hold (the near-field), the point multipole expansion is suboptimal for many practical calculations. For example, in atomistic molecular simulations, amino acids interacting inside a single protein are rarely more than several times $R_0$ apart. For these calculations, point multipoles can be expected to provide a suboptimal approximation of the original distribution.

We investigate an alternative to the point multipole expansion for approximating charge distributions – Optimal Physical Multipoles. Optimal Physical Multipoles approximate a charge distribution by a small number of point charges spatially distributed in an “optimal” way, to be precisely defined below. Since OPMs have a finite size, they may provide better representation of the original spatially extended charge distribution, i.e. a more accurate representation of the potential in the near-field. Consider for example the extreme case where the charge distribution consists of 6 charges of equal magnitude spaced equidistant on a line and alternating negative to positive (Figure 1). For such a distribution, an optimally placed point dipole still produces more than 25 times the average error produced by an Optimal Physical Dipole at a distance of $2R_0$ from the center of geometry of the original charge distribution. Furthermore, later we will prove that for at least the lowest order OPMs, i.e. Optimal Physical Monopole and Optimal Physical Dipole, OPMs are at least as accurate as an equivalent order point multipole. From a practical standpoint, Optimal Physical Multipoles may be easier to implement in applications that already utilize point
Figure 1: Relative errors in electrostatic potential around an example net neutral charge distribution consisting of 6 charges with equal magnitude spaced equidistant on a line and alternating negative to positive, see inset. An Optimal Physical Dipole produces less than 3.5% error for all angles (solid purple line), whereas an optimally placed point dipole produces over 45% error at some angles (dashed green line). The Optimal Physical Dipole consists of a negative and positive charge, of equal magnitude, placed on the left and right ends of the original charge distribution respectively. On the other hand, an optimally placed point dipole, as defined in [9, 17], is located at the center of geometry. The relative error is computed as
\[
\left( \frac{|\Phi(2R_0, \theta) - \Phi_{ref}(2R_0, \theta)|}{\sqrt{\frac{1}{4\pi} \int_0^{2\pi} \int_0^{\pi} (\Phi_{ref}(2R_0, \theta))^2 \sin(\theta) d\phi d\theta}} \right) \times 100\%
\]
where \( \Phi(2R_0, \theta), \Phi_{ref}(2R_0, \theta) \) are the electrostatic potentials of the approximate and the reference (original) charge distributions respectively. The electrostatic potentials are computed at a distance \( 2R_0 \) from the center of geometry, where \( 2R_0 \) is the size of the charge distribution (twice the distance from the center of geometry to the outermost charge in the original distribution).

Representing charge distributions by a small number of point charges is not by itself a novel idea. There are a number of methods, such as RESP [4], CHELP [6], CHELPG [5], CHELMO [19], coarse graining [3, 12, 2] and others [23] that empirically fit a set of point charges to a given charge distribution by minimizing various error metrics in electrostatic potential over some volume or surface surrounding the charge distribution. A key difference between these methods and Optimal Physical Multipoles introduced here is that OPMs inherit...
the physically appealing asymptotic properties of the point multipole approximation, i.e. the error in potential falls off at least as fast as $1/R^{k+1}$, where $R$ is the distance from the origin and $k$ is the highest order of the multipole terms retained in the expansion.

The rest of this work is organized as follows. We first review the multipole expansion concept. Next, we describe the theoretical basis for Optimal Physical Multipoles. We then use this theoretical formalism to derive closed-form expressions for the Optimal Physical Monopole and Dipole, discuss their properties and compare their accuracy with the corresponding point multipoles. Finally we provide a cost-benefit analysis of Optimal Physical Multipoles versus the point multipole method and discuss the prospect of expansions to higher orders. Potential uses and future work is discussed in “Conclusions”. Although point multipoles have been used to study a wide range of potentials, this proof-of-concept study focuses on just one of the most common application of the concept - electrostatics. Nevertheless, we believe that the ideas presented here will be generally applicable to other $1/R$, Coulomb-like, potentials as well.

2 Multipole Expansion

Here we will give a brief overview of the familiar formalism of the point multipole expansion. Since many practical applications, such as molecular dynamics simulations, use point charges, for notational simplicity we will consider discrete charge distributions, but the results also hold for continuous distributions.

Consider a set of $N$ point charges $q_n$ ($n = 1, 2, ..., N$) located at positions $r_n$ around some chosen origin. Then the potential $\Phi(R)$, of this distribution at a point $R$ from that origin is given by the familiar Coulomb Potential

$$\Phi(R) = \frac{1}{4\pi\epsilon_0} \sum_{n=1}^{N} \frac{q_n}{||R - r_n||}$$  \hspace{1cm} (1)

For distances $R > R_0$ where $R = ||R||$ and $R_0 = max(||r_n||)$, a Taylor series expansion of the potential above gives the classic multipole expansion. In Cartesian coordinates we obtain

$$\Phi(R) = \frac{1}{4\pi\epsilon_0} \left( \frac{1}{R} q + \frac{1}{R^2} \sum_{i=x,y,z} \hat{R}_i p_i + \frac{1}{R^3} \sum_{i,j=x,y,z} \hat{R}_i \hat{R}_j Q_{ij} 
+ \frac{1}{6} R^4 \sum_{i,j,k=x,y,z} \hat{R}_i \hat{R}_j \hat{R}_k O_{ijk} + \ldots \right)$$  \hspace{1cm} (2)

where

$$q = \sum_{n=1}^{N} q_n$$  \hspace{1cm} (3)
\[ p_i = \sum_{n=1}^{N} q_n r_{n,i} \]
\[ Q_{i,j} = \frac{1}{2} \sum_{n=1}^{N} q_n \left( 3r_{n,i}r_{n,j} - (r_n)^2 \delta_{ij} \right) \]
\[ O_{i,j,k} = \sum_{n=1}^{N} q_n \left( 15r_{n,i}r_{n,j}r_{n,k} - 3(r_n)^2 (r_{n,i}\delta_{jk} + r_{n,j}\delta_{ik} + r_{n,k}\delta_{i,j}) \right) \]

and \( q, p, Q, O \) are known as the monopole, dipole, quadrupole and octupole moments respectively, and \( \delta_{ij} \) is the Kronecker delta. The multipole moments are symmetric tensors where the lowest order non-vanishing multipole is origin independent.

3 Definition of Optimal Physical Multipoles

For a given set of original charges \( q_i \) \((i = 1, 2, \ldots, N)\), we want to determine a smaller representative set of charges \( \bar{q}_k \) \((k = 1, 2, \ldots, K < N)\) such that the potential due to these representative charges, \( \Phi(R) \) best approximates the potential of the original distribution, \( \Phi(R) \). In the following sections, we will outline the general method for determining this optimal set of representative charges, i.e. the Optimal Physical Multipole representation.

3.1 The Error Metric

Determining the best representative charge distribution is critically contingent upon the definition of the error metric used. In general we are concerned with obtaining the best representation of the original potential at any arbitrary point in space outside the distribution. Thus, for the error metric, \( \Delta \), one typically chooses the root mean square (RMS) of the error in potential over some volume \( V \) excluding the volume \( V_0 \) containing the charge distribution being approximated, i.e.

\[ \Delta^2 = \frac{1}{V \notin V_0} \int_{V \notin V_0} \left| \Phi(R) - \Phi(R) \right|^2 dV \]

In principle, one can derive the optimal charge placement \( \{ \bar{q}_n, \bar{r}_n \} \) by minimizing the integral given in Eq. (7) with respect to the values of the new charges, \( \{ \bar{q}_n \} \) and their positions \( \{ \bar{r}_n \} \). However, as the number of charges in the representative distribution grows, this equation can be difficult to minimize, let alone to find closed-form, analytic expressions for the placement and magnitude of the charges composing the representative distribution. Furthermore, charges chosen in this manner are not guaranteed to have the same multipole moments as the original distribution [19]. This can lead to misinterpretation of the properties of the distribution and, potentially, to unphysical results. At the very least, we would like the new representation to inherit the same transparent
asymptotic behavior of the corresponding point multipole expansion, but with
greater accuracy expected from an extended distribution that can better mimic
the original. To simplify the problem, we recast Eq. (7) in spherical coordinates
and consider the error inside a spherical shell centered on the chosen multipole
expansion center, and with arbitrary outer radius \( \tilde{R} > R_0 \), where \( R_0 \) is defined
as before, i.e. the distance from the expansion center to the outermost point
charge. The error metric now becomes

\[
\Delta^2 = \frac{3}{4\pi(R^3 - R_0^3)} \int_{R_0}^{\tilde{R}} \int_0^{2\pi} \int_0^\pi \left| \Phi(R) - \bar{\Phi}(R) \right|^2 R^2 \sin(\theta) d\theta d\phi dR
\]

where \( \theta \) and \( \phi \) are the usual spherical coordinate inclination and azimuth angles.

In spherical coordinates, the multipole expansion is given by

\[
\Phi(R) = \frac{1}{\epsilon_0} \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} \frac{1}{2\ell + 1} \frac{Y^m_\ell(\theta, \phi)}{R^{\ell+1}} q^m_\ell
\]

where \( Y^m_\ell \) are the standard spherical harmonics, \( * \) is the complex conjugate, \( q^m_\ell \)
are the spherical multipole moments, and \( \ell \) is the multipole order.

\[
q^m_\ell = \sum_{n=1}^{N} q_n r_n Y^m_\ell(\theta_n, \phi_n)^*
\]

Using this expansion as our error metric, Eq. (8), becomes

\[
\Delta^2 = \frac{3}{4\pi(\tilde{R}^3 - R_0^3)} \int_{R_0}^{\tilde{R}} \int_0^{2\pi} \int_0^\pi \left| \sum_{\ell=0}^{\infty} \sum_{m=-\ell}^{\ell} \frac{1}{2\ell + 1} \frac{Y^m_\ell(\theta, \phi)}{R^{\ell+1}} (q^m_\ell - \bar{q}^m_\ell) \right|^2 R^2 \sin(\theta) d\theta d\phi dR
\]

where \( q^m_\ell \) and \( \bar{q}^m_\ell \) are the spherical moments of the original and representa-
tive charge distributions respectively. Since the spherical harmonic integral
\[
\int_0^{2\pi} \int_0^\pi |Y^m_\ell(\theta, \phi)|^2 \sin(\theta) d\theta d\phi = 1,
\]
Eq. (11), can be further simplified to the following form [17],

\[
\Delta^2 = \frac{3}{4\pi\epsilon_0(\tilde{R}^3 - R_0^3)} \int_{R_0}^{\tilde{R}} \sum_{\ell=0}^{\infty} \frac{1}{(2\ell + 1)^2 R^{2\ell+1}} \sum_{m=-\ell}^{m=\ell} |q^m_\ell - \bar{q}^m_\ell|^2 dR
\]

From the structure of Eq. (12) we see that minimizing the difference between
the successive multipole moments of the original and Optimal Physical Multipole
distributions is equivalent to minimizing the total error, i.e. by minimizing
each term in the error expansion we minimize the RMS error in electrostatic
potential. Note that the procedure does not depend on the parameter \( \tilde{R} \), and
thus the method does not require explicit integration over a given region. The
use of the multipole expansion in this way allows for the sought after distinct separation of terms by the rate at which they decrease as a function of $R$, i.e. the monopole term falls off as $1/R$, the dipole falls off as $1/R^2$, etc. A representation which makes terms up to order $k$ in Eq. (12) equal to zero will produce total error whose leading term falls off as $1/R^{k+1}$.

3.2 Optimal Physical Multipole Approximation

We define an Optimal Physical Multipole of order $k$ to be a set of charges satisfying the following conditions:

1. It is the smallest set of point charges which make every term in the error expansion, Eq. (12), through order $k$ equal to zero (for the given charge distribution being approximated).

2. If the charge magnitudes and positions are not uniquely determined by condition 1, the charges are chosen such that the $k + 1, k + 2, \ldots$ terms in the error expansion are sequentially globally minimized until all the charges are uniquely defined.

Optimal Physical Multipoles as defined above have the useful property that for any point charge distribution they will, at some order $k$, reproduce the original point charge distribution. For, at some order $k$, the OPM will require the same number of charges $N$ as the original distribution to satisfy the first condition of the Optimal Physical Multipole definition. Furthermore, the OPM must be made identical to the original distribution to satisfy condition 2 from the definition above. To see how this arises note that the error expansion contains terms of the form $(q_{m}^{\ell} - \overline{q}_{m}^{\ell})^2$. Thus, an Optimal Physical Multipole which is identical to the original distribution will have $\overline{q}_{m}^{\ell} = q_{m}^{\ell}$ for all $\ell, m$ and clearly having $\overline{q}_{m}^{\ell} = q_{m}^{\ell}$ for all $m$ will be a global minimum of the error expansion term of order $\ell$. Since making the OPM identical to the original distribution will always provide a global minimum to all orders, setting the OPM equal to the original distribution provides the only way to place the charges such that they satisfy the second condition defining an OPM. We note that the convergence of Optimal Physical Multipoles to the original distribution after a finite number of computations sets OPMs apart from point multipole expansions which generally require an infinite number of terms to exactly reproduce a given charge distribution.

The minimizations of the error metric in Eq. (12) which are required to define an Optimal Physical Multipole can be done numerically to arbitrary order. This numeric procedure for calculating the Optimal Physical Multipole representation may be particularly useful in situations where the charge distributions are relatively static and thus the optimal representation does not need to be recalculated at each time step of a given simulation. Ideally, however, one would like analytic expressions that can be used to compute OPMs at a reduced computational cost.
4 Analytic Expressions for Low Order Optimal Physical Multipoles

In the following sections, we apply the general methodology developed in section 3, to derive low order OPMs and test their accuracy. In sections 4.1 and 4.2, we obtain analytic forms for the lowest order Optimal Physical Multipoles in two important special cases, namely, we define the Optimal Physical Monopole for systems with non-zero charge and the Optimal Physical Dipole for systems with zero charge but non-zero dipole moment. These analytic expressions not only provide physical insight but are more computationally efficient than the numerical minimization procedures that are in general required to obtain an approximate charge distribution. Thus, these analytic expressions may be particularly useful in applications such as molecular dynamics where computational speed is critical.

4.1 Optimal Physical Monopole

The Optimal Physical Monopole, order \( k = 0 \), consists of a single charge. As long as the single charge has magnitude \( \bar{q} = q \), i.e. is equal to the total charge of the original distribution, the monopole term of the error expansion will obviously be zero. Thus, any charge with magnitude equal to the net charge of the original distribution will satisfy the first condition which defines a Optimal Physical Multipole. Now, the remaining parameters, namely the position of the charge, are chosen to satisfy condition 2 of the Optimal Physical Multipole definition, namely to minimize the dipole term in the error expansion. In this particular case, the \( k + 1 \) term of the error, i.e. the dipole term, can be made identically zero by solving

\[
\begin{align*}
px - \bar{q} \cdot x &= 0 \\
py - \bar{q} \cdot y &= 0 \\
pz - \bar{q} \cdot z &= 0
\end{align*}
\]

for \( x, y, z \) where \( px, py, pz \) are the \( x, y, z \) components of the dipole moment \( p \) of the original distribution. Solving the above equations we have

\[
\bar{q} = q
\]

\[
\bar{r} = \frac{p}{q}
\]

So, a charge of magnitude \( \bar{q} \) placed at \( \bar{r} \) satisfies both conditions which define Optimal Physical Multipole of order \( k = 0 \).

The Optimal Physical Monopole can offer substantial improvements compared to the use of a single charge placed at the common choice of the geometric center. In particular, there are biologically relevant examples, see Fig. 2, where a point monopole at the origin produces an RMS error 5 times greater than that of the proposed Optimal Physical Monopole.
Figure 2: Relative error in electrostatic potential produced by an Optimal Physical Monopole representing the charge distribution of an amino acid that carries a net charge of $+1|e|$ (glutamic acid at physiological pH). The inset image shows the plane bisecting the molecule which defines the angle plotted in the figure; to illustrate the original charge distribution, the electrostatic potential of the glutamic acid is plotted on its molecular surface as a color map with blue representing positive and red representing negative potential [8]. The relative error is computed as in Fig. 1, (ratio of the absolute error to the RMS average of the reference potential), at a distance $2R_0$ which as before is twice the distance from the center of geometry to the outermost charge. The Optimal Physical Monopole, located at the center of charge, produces less than 11% error (solid purple line) for all angles whereas the point monopole, located at the center of geometry, produces over 45% error (dashed green line) for some angles.

Despite its similarity to the center of mass, the existence of negative charge makes the center of charge term fundamentally different from center of mass. In particular, as the total charge in the distribution approaches zero, the center of charge tends towards infinity. However, in practice, charge is discrete, so there is a limit to the maximum distance the center of charge can fall outside of a given distribution.

4.2 Optimal Physical Dipole

For an uncharged distribution, the Optimal Physical Dipole consists of two charges $\tilde{q}_1 = \tilde{q}$ and $\tilde{q}_2 = -\tilde{q}$ located at positions $\tilde{r}_1$ and $\tilde{r}_2$ respectively. Thus,
it takes 7 parameters to uniquely define an Optimal Physical Dipole. By setting

$$\vec{q}(\vec{r}_1 - \vec{r}_2) = \sum_{n=1}^{N} q_n r_n \quad (18)$$

the dipole term in the error is zero and the two charges satisfy condition 1 of the Optimal Physical Dipole definition. Now, we will rewrite the positions $\vec{r}_1$ and $\vec{r}_2$ in the following form:

$$\vec{r}_1 = \vec{d} + \frac{\sum q_n r_n}{2\vec{q}}$$
$$\vec{r}_2 = \vec{d} - \frac{\sum q_n r_n}{2\vec{q}} \quad (19)$$

where $\vec{d}$ represents the geometric center between the two charges. We can see that these positions satisfy relation (18) automatically. By writing the positions of the charges in this manner, we have divided the process of determining the remaining parameters which define the Optimal Physical Dipole into two steps, namely, finding the optimal placement of the charges, $\vec{d}$, and finding the optimal magnitude of the charge, $\vec{q}$. Note that finding the optimal charge value fixes the separation between the two charges, since the dipole moment of the representative distribution has been constrained to equal the original dipole moment.

The placement of the geometric center of the charges composing the Optimal Physical Dipole, $\vec{d}$, that minimizes the quadrupole term of the error expansion is given by

$$\vec{d}_k = \frac{2}{3p^2} \left( \sum_{i=x,y,z} Q_{ki} p_i - \left( \frac{\sum_{i,j=x,y,z} Q_{ji} p_i p_j}{4p^2} \right) p_k \right) \quad (20)$$

where $k = x, y, z$ and thus the $\vec{d}_k$’s are the components of $\vec{d}$. This optimal position, known as the center of dipole, was derived previously [17] for a different purpose, namely for matching point multipole expansions between different charge distributions. Now, unlike the point dipole, the Optimal Physical Dipole has physical size and thus an additional parameter with which to further minimize the error with respect to the given potential. In other words, Eqs. (20) and (18), determine only 6 of the 7 parameters required to define an Optimal Physical Dipole. Since the quadrupole moment is the lowest order non-zero term remaining in the error expansion, by choosing the optimal charge value, we want to further minimize the quadrupole term in the error. However, for any charge value $\vec{q}$ an Optimal Physical Dipole placed at the center of dipole has no quadrupole moment as can be seen by setting $N = 2$, substituting the center of dipole, Eq. (20) and $q_1 = -q_2 = \vec{q}$ into Eq. (19) then substituting these variables into Eq. (6). Thus, the quadrupole term in the error, Eq. (12) is unaffected by the choice of the charge magnitude, $\vec{q}$ and the quadrupole term
Figure 3: Relative error in electrostatic potential produced by Optimal Physical Dipole representing charge distribution of an amino acid that carries a zero net charge (C-terminal arginine at physiological pH). The inset image shows the plane bisecting the molecule defining the angle plotted in the figure; to illustrate the original charge distribution, the electrostatic potential of the arginine is plotted on its molecular surface as a color map with blue representing positive and red representing negative potential [8]. The relative error is computed as in Fig. 1, (ratio of the absolute error to the RMS average of the reference potential), at a distance $2R_0$, which as before is twice the distance from the center of geometry to the outermost charge. The Optimal Physical Dipole produces less than 5% error (solid purple line) for all angles, whereas the optimally placed, see [9, 17], point dipole produces over 30% error (dashed green line) for some angles.

has already been globally minimized. Therefore, to uniquely define the charge, $\bar{q}$, we follow the OPM definition and globally minimize the next term in the error expansion, namely the octupole term. Specifically, if we consider the $\ell = 3$ term of Eq. (12), using the connection formula from spherical multipoles to Cartesian multipoles we can compute

$$\sum_{i,j,k=x,y,z} \frac{\partial}{\partial \bar{q}} (O_{ijk} - \overline{O_{ijk}})^2 = 0$$

(21)

where $O_{ijk}$ and $\overline{O_{ijk}}$ are the octupole moments, in Cartesian coordinates, of the original distribution and the Optimal Physical Dipole respectively, for an expansion computed about the center of dipole. Now, by noting that $\overline{O_{ijk}}$ is a function of $\bar{q}$, we find that Eq. (21) is satisfied when $\bar{q} \to \infty$ or if the charge
value is given by
\[
\bar{q} = \sqrt{\frac{3p^6}{2 \sum_{i,j,k=x,y,z} O_{ijk}p_ip_jp_k}} \quad (22)
\]
Thus, Eqs. (19), (20) and (22) define the Optimal Physical Dipole, i.e. defines the best placement of charges such that RMS error on a sphere centered at the center of dipole is minimized. For certain charge distributions relevant to molecular biophysics, the Optimal Physical Dipole produces error several times lower than that of the corresponding a point dipole, see Fig. 3.

Although the Optimal Physical Dipole can produce dramatically lower error than the point dipole, it is possible that
\[
\sum_{i,j,k=x,y,z} O_{ijk}p_ip_jp_k \leq 0 \quad (23)
\]
In this case, the charge given by Eq. (22) is imaginary. This situation occurs when the orientation of the dipole with respect to the octupole is such that increasing the distance between the charges of the Optimal Physical Dipole always increases the error. Thus, Eq. (21) is formally satisfied only for \( \bar{q} \to \infty \). In a practical calculation, a physical dipole with the above property is constructed by fixing the separation between the charges \( ||\bar{r}_1 - \bar{r}_2|| \) to a very small value, while increasing the charge accordingly to maintain the original dipole moment. In these cases, the Optimal Physical Dipole does not offer an advantage over the optimal point dipole, however, the Optimal Physical Dipole can always mimic the point dipole to arbitrary precision and thus the two distributions will produce equivalent error. Thus, even if inequality (23) holds, the Optimal Physical Dipole represents the optimal placement of two point charges and is at least as accurate as the point dipole.

Curiously, the most biologically important molecule, water, satisfies inequality (23). Thus, among point charge representations that use only two charges to approximate the true charge density distribution of water molecule, the most accurate electrostatic potential outside of the original charge distribution is produced by two charges that mimic a point dipole placed at the center of dipole, that is itself a special case of the Optimal Physical Dipole with \( ||\bar{r}_1 - \bar{r}_2|| \to 0 \). Other two-charge charge models that may appear more ‘intuitive’ by keeping the charge-charge distance comparable to the size of the system, i.e. water, are bound to produce less accurate representations of the electrostatic potential of the original charge distribution. For example, the model used in [12], places a \(-0.7|e|\) charge on the oxygen and \(+0.7|e|\) at the geometric center of the two hydrogens. However, this ‘intuitive’ dipole solution produces 20% more error at positions near the hydrogen atoms and overall produces \( \sim 10\% \) higher RMS error compared to Optimal Physical Dipole solution (when integrated over a sphere of radius \( 2R_0 \)), see Fig. 4. We stress that the above accuracy analysis is strictly limited to electrostatics; other considerations may dictate electrostatically suboptimal placements of point charges in coarse-grained models of water.
Figure 4: Relative error in computed electrostatic potential for a water molecule: Optimal vs. ‘intuitive’ Physical Dipole. The reference charge density of the electron distribution for water was calculated using the CCSD method with aug-cc-pCVTZ basis set \[7, 14, 24\] at experimental equilibrium geometry of water in vacuum. The electron distribution is confined to a box with a side length of \(4a_0\); the discretization is \(0.1a_0\) along each axis, where \(a_0\) is the atomic unit of length (the Bohr Radius). Here, the Optimal Physical Dipole consists of a negative and positive charge with magnitude \(10|e|\) whose center is offset by 0.070\(a_0\) from the oxygen nucleus toward the protons along the water symmetry axis. The charges are separated by 0.074\(a_0\) to maintain the original dipole moment of water. The ‘intuitive’ dipole representation, places a positive charge, with magnitude 0.7\(|e|\), at the geometric center between the protons and a negative charge \((-0.7|e|)\) on the oxygen. The relative error is computed as in Fig. 1, (ratio of the absolute error to the RMS average of the reference potential), at a distance \(2R_0\) which in this case has been defined to be 5 times the OH distance from the center of the quantum electron charge distribution. Along some directions, e.g., at \(\theta = 0 = 2\pi\), the Optimal Physical Dipole produces error 6 times smaller than that of the ‘intuitive’ dipole. Overall, the average RMS error of the potential due to the Optimal Physical Dipole is 10\% smaller than that due to the ‘intuitive’ dipole.

5 Cost Benefit Analysis

Whether the OPMs introduced in the preceding sections will be a beneficial simplification in practice will depend upon the specifics of the application. Physical multipoles may be easier to implement than point multipoles in applications that already utilize point charges, such as many molecular dynamics codes. Furthermore, the lowest order Optimal Physical Multipoles have been shown to be
always at least as accurate as the corresponding point multipole and in certain distributions may be substantially more accurate than an equivalent point multipole. We conjecture that the accuracy advantage for some practically useful distributions also holds for higher order OPMs.

One of the major advantages in using the Optimal Physical Multipole method versus point multipoles comes in at the level of pairwise interactions. Note that although Cartesian formalisms exist for the calculation of pairwise interactions \[15\], we will restrict the following discussion to the more commonly used spherical formalism. Consider two systems of charges, one containing of \(N_A\) charges \(\{q_i\}\) located at \(\{r_i\}\) clustered around an origin located at \(R_A\) and another containing of \(N_B\) charges \(\{q_j\}\) located at \(\{r_j\}\) clustered around an origin located at \(R_B\). Then the interaction energy between the two systems is given by

\[
U_{AB} = \sum_{i=1}^{N_A} \sum_{j=1}^{N_B} \frac{q_i q_j}{4\pi\epsilon_0 ||r_i - r_j||}
\]

(24)

Thus, the interaction requires \(N_A N_B\) computations. So, for large charge distributions the computation scales as \(O(N^2)\). Now, using the point multipole expansion, this interaction energy becomes \(22\)

\[
U_{AB} = \frac{1}{\epsilon_0} \sum_{\ell_A=0}^{\infty} \sum_{\ell_B=0}^{\infty} (-1)^{\ell_B} \left( \frac{2\ell_A + 2\ell_B}{2\ell_A} \right)^{1/2} \frac{1}{\sqrt{(2\ell_A + 1)(2\ell_B + 1)}} \\
\times \sum_{m_A=-\ell_A}^{\ell_A} \sum_{m_B=-\ell_B}^{\ell_B} \left( I_{\ell_A+\ell_B}^{-m_A-m_B}(R_{AB}) \right) \\
q_{\ell_A}^{m_A} q_{\ell_B}^{m_B} \langle \ell_A, m_A; \ell_B, m_B|\ell_A + \ell_B, m_A + m_B \rangle
\]

(25)

for the irregular spherical harmonic, \(I_{\ell_A+\ell_B}^{-m_A-m_B}(R_{AB})\), given by

\[
I_{\ell_A+\ell_B}^{-m_A-m_B}(R_{AB}) = \left( \frac{4\pi}{2\ell_A + 2\ell_B + 1} \right)^{1/2} \frac{Y_{\ell_A+\ell_B}^{-(m_A+m_B)}(\hat{R}_{AB})}{R_{AB}^{\ell_A+\ell_B+1}}.
\]

(26)

where \(R_{AB} = ||R_A - R_B||\), \(\hat{R}_{AB}\) is the unit vector in the direction of \(R_{AB}\) and the bracketed expression is the Clebsch-Gordan Coefficient. This expression has the benefit of scaling linearly with the number of charges. However, the number of computations required to compute the pairwise interaction energy between two distributions scales as \(O(\ell^3)\) with the number, \(\ell\) of point multipole terms in the interaction. In particular, to determine the interaction energy between two charge distributions each with zero net charge but non-zero dipole moment requires the calculation of 9 terms, namely the dipole-dipole interaction term. On the other hand, an equivalent Optimal Physical Dipole representation requires only 4 calculations. To determine the interaction energy of a system with non-zero monopole, dipole and quadrupole moments, a scheme
based on point multipoles would require, in general, 84 terms, namely the various monopole-monopole, monopole-dipole, monopole-quadrupole, dipole-dipole, dipole-quadrupole and quadrupole-quadrupole terms. On the other hand, the interaction energy of two Optimal Physical Quadrupoles, containing 5 charges each, requires only 25 terms. Additionally, the Coulomb interaction, used to compute the interaction between Optimal Physical Multipoles, does not require the computation of spherical harmonics or Clebsch-Gordan coefficients, which may be cumbersome. Thus, using Optimal Physical Multipoles has a computational advantage over spherical point multipoles when calculating interaction energies. We have kept the above discussion at the most general level – specific symmetries present in the original charge distribution may change the numbers.

6 Conclusion

Point multipole expansion is a widely used approach to simplify and approximate potentials and fields around complex charge distributions via power series. However, in practical calculations which typically retain only a few leading terms, the approximation can lead to inaccurate results in the near-field. In this work, we have introduced an alternative to the point multipole expansion for approximating the electrostatic potential of a charge distribution, namely, Optimal Physical Multipoles (OPMs). An OPM consists of a set of point charges which are optimally placed to best reproduce the original charge distribution at a given multipole order. Namely, the OPM exactly reproduces the point multipole expansion of the original distribution up to a given order while optimally approximating the remaining lowest order non-zero point multipole terms. Thus, by construction, OPMs retain many of the useful properties of point multipole expansions, in particular they retain the asymptotic behavior of the point multipole expansion. At the same time, an expansion based on OPMs can be more accurate than the point multipole expansion of the same order; for some charge distributions relevant to molecular biophysics (amin-acid) the accuracy gain is more than 5-fold in the near-field. At least for the lowest order OPMs (monopole and dipole), the expansion is guaranteed to be at least as accurate as the corresponding point multipole expansion of the same order. We have provided a general framework for calculating OPMs to any order and have derived closed-form expressions for the Optimal Physical Monopole and Dipole.

In comparison to point multipoles, expansions based on Optimal Physical Multipoles have many desirable properties that may be useful in practical computations; in particular, their mathematical form – the sum of contribution from point sources – is simpler than that of the conventional point multipole expansion. Thus, OPMs may be easier to implement into existing molecular dynamics protocols. At the same time, unlike many approximations based on point charge representations, OPMs are uniquely defined and preserve the natural hierarchy of the multipole features of the original charge distribution.

Optimal Physical Multipoles is a new concept; thus its many applications and potentially useful properties remain unexplored in this proof-of-concept
work. OPMs are expected to have utility in coarse-grained \cite{3, 13} and multi-scale methods \cite{2}, especially in dynamics \cite{1} where analytic expressions and the simplicity of the algorithms is key. The Optimal Physical Multipole framework provides a systematic way of deriving approximate charge distributions that have the potential to be both computationally effective and produce an accurate representation of the original electrostatic potential. To further improve the representation of the original potential via OPMs, future work may consider partitioning the original charge distribution into several domains, and finding OPMs for each of them separately, similar to the distributed multipoles approach \cite{10, 20, 21}. Further exploration of the mathematical and physical properties of OPMs is also desirable; future studies may reveal whether closed form solutions exist for higher order OPMs.

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References

[1] Ramu Anandakrishnan, Mayank Daga, and Alexey V. Onufriev. An n log n generalized born approximation. \textit{Journal of Chemical Theory and Computation}, 7(3):544–559, March 2011.

[2] Ramu Anandakrishnan and Alexey V Onufriev. An N log N approximation based on the natural organization of biomolecules for speeding up the computation of long range interactions. \textit{Journal of Computational Chemistry}, 31(4):691–706, March 2010.

[3] Nathalie Basdevant, Daniel Borgis, and Tap Ha-Duong. A coarse-grained protein-protein potential derived from an all-atom force field. \textit{Journal of Physical Chemistry. B}, 111(31):9390–9, August 2007.

[4] Christopher I. Bayly, Piotr Cieplak, Wendy Cornell, and Peter A. Kollman. A well-behaved electrostatic potential based method using charge restraints for deriving atomic charges: the RESP model. \textit{Journal of Physical Chemistry}, 97(40):10269–10280, October 1993.

[5] Curt M. Breneman and Kenneth B. Wiberg. Determining atom-centered monopoles from molecular electrostatic potentials. the need for high sampling density in formamide conformational analysis. \textit{Journal of Computational Chemistry}, 11(3):361–373, 1990.

[6] Lisa Emily Chirlian and Michelle Miller Francl. Atomic charges derived from electrostatic potentials: A detailed study. \textit{Journal of Computational Chemistry}, 8(6):894–905, 1987.
[7] T. H. Dunning. Gaussian basis sets for use in correlated molecular calculations. I. The atoms boron through neon and hydrogen. *Journal of Chemical Physics*, 90:1007, 1989.

[8] John C Gordon, Andrew T Fenley, and Alexey Onufriev. An analytical approach to computing biomolecular electrostatic potential. II. Validation and applications. *Journal of Chemical Physics*, 129(7):075102, August 2008.

[9] Apostol Gramada and Philip Bourne. Resolving a distribution of charge into intrinsic multipole moments: A rankwise distributed multipole analysis. *Physical Review E*, 78(6):1–7, December 2008.

[10] Apostol Gramada and Philip E Bourne. Coarse-graining the electrostatic potential via distributed multipole expansions. *Computer Physics Communications*, 182(7):1455–1462, July 2011.

[11] L Greengard and V Rokhlin. A fast algorithm for particle simulations. *Journal of Computational Physics*, 73(2):325–348, December 1987.

[12] Sergei Izvekov and Gregory A Voth. A multiscale coarse-graining method for biomolecular systems. *Journal of Physical Chemistry. B*, 109(7):2469–73, February 2005.

[13] Sergei Izvekov and Gregory A Voth. Multiscale coarse graining of liquid-state systems. *Journal of Chemical Physics*, 123(13):134105, October 2005.

[14] R. A. Kendall, T. H. Dunning, and R. J. Harrison. Electron-affinities of the 1st-row atoms revisited – systematic basis-sets and wave-functions. *Journal of Chemical Physics*, 96:6796, 1992.

[15] Yong (Washington University) Kong. *Multipole Electrostatic Methods for Protein Modeling with Reaction Field Treatment*. PhD thesis, Washington University, 1997.

[16] D Pearlman. AMBER, a package of computer programs for applying molecular mechanics, normal mode analysis, molecular dynamics and free energy calculations to simulate the structural and energetic properties of molecules. *Computer Physics Communications*, 91(1-3):1–41, September 1995.

[17] DE Platt and BD Silverman. Registration, orientation, and similarity of molecular electrostatic potentials through multipole matching. *Journal of Computational Chemistry*, 17(3):358–366, 1996.

[18] T. Schlick. *Molecular Modeling and Simulation: An Interdisciplinary Guide*. Interdisciplinary Applied Mathematics. Springer, 2010.

[19] Emma Sigfridsson and Ulf Ryde. Comparison of methods for deriving atomic charges from the electrostatic potential and moments. *Journal of Computational Chemistry*, 19(4):377, March 1998.
[20] A. J. Stone. Distributed multipole analysis, or how to describe a molecular charge distribution. *Chemical Physics Letters*, 83(2):233–239, October 1981.

[21] A. J. Stone and M. Alderton. Distributed multipole analysis. *Molecular Physics*, 56(5):1047–1064, December 1985.

[22] A. J. Stone and R.J.A. Tough. Spherical tensor theory of long-range intermolecular forces. *Chemical Physics Letters*, 110(2):123 – 129, 1984.

[23] Marcel Swart, Piet Th. van Duijnen, and Jaap G. Snijders. A charge analysis derived from an atomic multipole expansion. *Journal of Computational Chemistry*, 22(1):79–88, 2001.

[24] D. E. Woon and T. H. Dunning. Gaussian basis sets for use in correlated molecular calculations. V. Core-valence basis sets for boron through neon. *Journal of Chemical Physics*, 103:4572, 1995.