

Charge Model 5: An Extension of Hirshfeld Population Analysis for the Accurate Description of Molecular Interactions in Gaseous and Condensed Phases

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S Supporting Information

ABSTRACT: We propose a novel approach to deriving partial atomic charges from population analysis. The new model, called Charge Model 5 (CM5), yields class IV partial atomic charges by mapping from those obtained by Hirshfeld population analysis of density functional electronic charge distributions. The CM5 model utilizes a single set of parameters derived by fitting to reference values of the gas-phase dipole moments of 614 molecular structures. An additional test set (not included in the CM5 parametrization) contained 107 singly charged ions with nonzero dipole moments, calculated from the accurate electronic charge density, with respect to the center of nuclear charges. The CM5 model is applicable to any charged or uncharged molecule composed of any element of the periodic table in the gas phase or in solution. The CM5 model predicts dipole moments for the tested molecules that are more accurate on average than those from the original Hirshfeld method or from many other popular schemes including atomic polar tensor and Löwdin, Mulliken, and natural population analyses. In addition, the CM5 charge model is essentially independent of a basis set. It can be used with larger basis sets, and thereby this model significantly improves on our previous charge models CM x ($x = 1-4$ or 4M) and other methods that are prone to basis set sensitivity. CM5 partial atomic charges are less conformationally dependent than those derived from electrostatic potentials. The CM5 model does not suffer from ill conditioning for buried atoms in larger molecules, as electrostatic fitting schemes sometimes do. The CM5 model can be used with any level of electronic structure theory (Hartree–Fock, post-Hartree–Fock, and other wave function correlated methods or density functional theory) as long as an accurate electronic charge distribution and a Hirshfeld analysis can be computed for that level of theory.

1. INTRODUCTION

The molecular dipole moment (as well as all higher multipole moments) can be reproduced exactly using quantities derived from Hirshfeld population analysis;^{1–6} for the molecular dipole moment, this requires using the atomic charges and atomic dipoles.⁷ However, for many purposes in molecular modeling, one wants to use a simplified representation of the molecular charge distribution that involves only atomic charges, i.e., the distributed monopole approximation without higher multipole moments. If one uses only the charges from Hirshfeld analysis, the molecular dipole moment is reproduced less accurately and is usually underestimated. Our goal here is to develop a general scheme to map a molecule's Hirshfeld charges onto a new set of charges that provide a reasonable representation of the electrostatic potential for molecular modeling without the atomic dipoles. Since one may easily normalize the atomic charges to reproduce the total charge on the molecule, the leading error in the molecular charge distribution for molecules lacking inversion symmetry is the molecular dipole moment. Therefore, we will use the molecular dipole moment as the key quantity that the mapped charges should reproduce. We note that a model that gives accurate molecular dipole moments for small molecules should give accurate bond dipoles and hence accurate resultant molecular dipole moments for large molecules.

We recall here that various schemes for assigning charges in a molecule fall into four distinct categories.⁸ Class I charges are

derived by using nonquantum mechanical approaches such as classical models of dipoles⁹ or by using a model to extract the charges directly from experimental data,¹⁰ e.g., from the experimental dipole moment of a diatomic molecule. Class II charges are based on a partitioning of the electron charge density obtained from a quantum-mechanical calculation into atomic populations. For example, class II charges are those obtained using Hirshfeld population analysis¹ or iterative Hirshfeld population analysis,^{5,6,11} Mulliken population analysis,¹² Löwdin population analysis,^{13,14} natural bond orbital population analysis,^{15,16} atomic polar tensor-based population analysis,¹⁷ the theory of atoms in molecules,¹⁸ and population analysis in terms of “fuzzy” atoms;¹⁹ see also refs 20–22 (and references therein). As will be discussed below, charges obtained from population analysis may depend on level of theory, for example, on the choice of density functional and/or basis set, and they may yield an unrealistic representation of the molecular dipole moment and higher-order multipole moments in complex molecules.

Class III atomic charges are those fitted to reproduce a physical observable like a quantum-mechanically calculated electrostatic potential (ESP),²³ for example, ESP charges obtained by the methods of Kollman and co-workers,^{24,25} Chirlian and Francl,²⁶ or Breneman and Wiberg;²⁷ see also

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ref 28 and references therein. In general, ESP-derived charges depend on the molecular coordinate system orientation and the choice of fitting points, and they sometimes exhibit an unphysical dependence on internal bond rotations, and their determination can also suffer from ill conditioning for interior (or buried) atoms in molecules, especially larger ones.^{27,29–32} These deficiencies of class III charges can be mitigated by using restrained electrostatic potential (RESP) fitting and introducing other refinements, for example, in the point selection algorithm.^{27,29–32}

Finally, class IV atomic charges are those defined through parametrization to reproduce accurately charge-dependent observables (such as dipole moments) obtained from experimental results or from high-level quantum mechanical calculations that are acceptably converged for the quantity under consideration.⁸ Examples of class IV charges are those based on Charge Model 1 (CM1)⁸ or on CM2,³³ CM3,^{34–36} CM4,³⁷ or CM4M.³⁸

The CM x charge models ($x = 1–4$ or 4M) were designed to yield atomic charges that overcome the disadvantages of class II and class III charges mentioned above. The CM x models map class II charges from Löwdin population analysis¹³ or redistributed Löwdin population analysis³⁹ onto new sets of charges (class IV) using simple functional forms parametrized for various combinations of density functionals and basis sets to accurately reproduce the reference dipole moments for a large number of polar molecules (for example, the CM4M training set includes 397 reference dipole moments). Since the CM x models use individual sets of model parameters optimized for different computational methods, the CM x charges are less sensitive to a level of theory than the corresponding Löwdin charges. The dipole moments calculated using CM x charges are more accurate on average than those obtained from class II charges.³⁸ Unlike class III charges, the class IV CM x charges are not derived from electrostatic potentials, and therefore they do not suffer *a priori* from ill conditioning for buried atoms or conformational dependence. A major limitation of the existing CM x models based on the mapping of Löwdin charges is that they were optimized at most for 10 relatively small basis sets where 6-31+G(d,p) is the largest one.³⁸ An extension of the existing CM x models (for example, CM4M) to larger basis sets (for example, to a basis of triple- ζ quality) is not advisable because the accuracy of Löwdin charges deteriorates rapidly upon increasing the number of basis functions (as will be reconfirmed later), and the accuracy of Mulliken charges sometimes deteriorates even more rapidly with basis set size.⁴⁰

In this article, we present a new charge model called Charge Model 5 (CM5). Unlike the earlier CM x models,^{8,33–38} this model yields class IV atomic charges derived from the Hirshfeld population analysis charges rather than from Mulliken, Löwdin, or redistributed Löwdin charges. We find that Hirshfeld charges are less sensitive to basis set size or the choice of basis as compared to those from other population analyses surveyed, making it possible to create a new model that uses a single set of model parameters that depend neither on the electronic structure method nor on the basis set. The CM5 model also improves on the most recent CM x model (CM4M) by using a larger and more diverse training set that includes 614 reference data versus 397 data in the CM4M training set.³⁸ Moreover, the CM5 model was parametrized using the data for 26 elements (namely, H–Ca, Zn, Ge–Br, and I) in a way designed to allow it to be extended to the whole periodic table, and it has been so

extended, whereas the CM4M model is only applicable to molecules containing H, Li, C, N, O, F, Si, P, S, Cl, and/or Br.

2. COMPUTATIONAL DETAILS

2.1. The CM5 Formalism. In the CM5 model, atomic charges in a molecule (either neutral or ionic) are defined by the following equations:

$$q_k^{\text{CM5}} = q_k^{\text{HPA}} + \sum_{k' \neq k} T_{kk'} B_{kk'} \quad (1)$$

$$B_{kk'} = \exp[-\alpha(r_{kk'} - R_{Z_k} - R_{Z_{k'}})] \quad (2)$$

where the indexes k and k' run over all atoms in the molecule, Z_k and $Z_{k'}$ are the corresponding atomic numbers, R_Z is the atomic covalent radius tabulated in ref 41 based on the data from refs 42 and 43, and q_k^{HPA} is the partial atomic charge from Hirshfeld population analysis^{1–3} (HPA). The quantities α and $T_{kk'}$ (where $T_{kk'} = -T_{k'k}$) are model parameters to be determined. The quantity $B_{kk'}$ defined by eq 2 will be called the Pauling bond order in this work because a similar equation was proposed by Pauling (see eq 1 in ref 44).

If the atomic number Z_k equals 1, 6, 7, or 8, and the atomic number $Z_{k'}$ also equals 1, 6, 7, or 8, the T coefficients are defined as

$$T_{kk'} = D_{Z_k Z_{k'}} \quad (3)$$

where $D_{Z_k Z_{k'}}$ is a pairwise parameter depending on the atomic numbers of atoms k and k' , and $D_{Z_k Z_{k'}} = -D_{Z_{k'} Z_k}$ and $D_{Z_k Z_k} = 0$ if $Z_k = Z_{k'}$. For convenience of discussion and tabulation, we usually replace the atomic number with the atomic symbol, e.g., we say $D_{\text{H-C}}$ instead of D_{16} . Thus, the set of all pairwise values $D_{Z_k Z_{k'}}$ is defined by $D_{\text{H-C}}$, $D_{\text{H-N}}$, $D_{\text{H-O}}$, $D_{\text{C-N}}$, $D_{\text{C-O}}$, and $D_{\text{N-O}}$. For all other cases, the T coefficients are defined as

$$T_{kk'} = D_{Z_k} - D_{Z_{k'}} \quad (4)$$

where the atomic parameters D_{Z_k} and $D_{Z_{k'}}$ are members of a set of D_Z defined for all atomic numbers Z of the periodic table.

2.2. The CM5 Parameterization. The CM5 model was parametrized using five electronic structure methods (namely, the five density functionals M06-L,^{45,46} M06,^{46,47} M06-2X,^{46,47} B3LYP,^{48–51} and mPW1PW⁵²). With these density functionals, we used the MG3S basis set^{53,54} for all parametrized elements with a few exceptions specified in section 2.4. Note that the MG3S basis set is identical to 6-311+G(3d2f,2df,2p)^{55–57} for elements with atomic numbers of 14 or lower.

The CM5 model was parametrized using a training set of 614 compounds composed of elements H–Ca, Zn, Ge–Br, and I and using the following constraints:

$$D_{\text{Li}} = D_{\text{Mg}} = D_{\text{Ca}} = D_{\text{Zn}} = 0 \quad (5)$$

$$D_{\text{C}} = D_{\text{H}} - D_{\text{H-C}} \quad (6)$$

$$D_Z = CD_{Z'} \quad (7)$$

In eq 7, the atomic symbol Z refers to Ne, Al, P, S, Cl, Ar, K, Ge, As, Se, Br, or I, and the atomic symbol Z' denotes the element preceding the element Z in the same group of the periodic table (for example, $Z' = \text{F}$ for $Z = \text{Cl}$, $Z' = \text{Cl}$ for $Z = \text{Br}$, etc.). The reason for eq 5 is that preliminary work showed that the optimum value of these four parameters is so close to zero that the deviation from zero is not meaningful. Thus, there are 17 independent nonzero parameters to be optimized, in

Table 1. CM5 Parameters for H–Ca, Zn, Ge–Br, and I^{a,b}

atom-wise			atom-wise (cont.)			pairwise		
Z	D_Z	N_Z	Z	D_Z	N_Z	Z–Z'	$D_{ZZ'}$	$N_{ZZ'}$
H	0.0056	481	Si	−0.0790	50	H–C	0.0502	369
He	−0.1543	10	P	−0.0756 ^c	47	H–N	0.1747	53
Li	0 ^c	22	S	−0.0565 ^c	71	H–O	0.1671	50
Be	0.0333	16	Cl	−0.0444 ^c	93	C–N	0.0556	95
B	−0.1030	16	Ar	−0.0767 ^c	11	C–O	0.0234	103
C	−0.0446 ^d	396	K	0.0130 ^c	16	N–O	−0.0346	18
N	−0.1072	134	Ca	0 ^c	12			
O	−0.0802	169	Zn	0 ^c	18			
F	−0.0629	109	Ge	−0.0557 ^c	14			
Ne	−0.1088 ^c	10	As	−0.0533 ^c	15			
Na	0.0184	19	Se	−0.0399 ^c	18			
Mg	0 ^c	16	Br	−0.0313 ^c	28			
Al	−0.0726 ^c	12	I	−0.0220 ^c	15			

^aThese parameters were optimized as independent unless noted otherwise. The Z index refers to an atomic symbol. D_Z and $D_{ZZ'}$ are dimensionless. N_Z indicates the number of molecules in the training set of 614 molecular configurations that contain Z. $N_{ZZ'}$ indicates the number of molecules that contain one or more Z–Z' chemical bonds (defined for this tabulation as interactions with Pauling bond order greater than 0.2). Values of the CM5 parameters extended to the whole periodic table are listed in the Supporting Information. ^bThere are two additional parameters: $\alpha = 2.474$ (Å^{−1}) and $C = 0.705$. ^cDetermined using eq 5. ^dDetermined using eq 6. ^eDetermined using eq 7.

particular, D_H , D_{He} , D_{Be} , D_B , D_N , D_O , D_F , D_{Na} , D_{Si} , D_{H-C} , D_{H-N} , D_{H-O} , D_{C-N} , D_{C-O} , D_{N-O} , C , and α (the latter is used in eq 2). These parameters were optimized using a multistep optimization procedure outlined below.

At the first step (step 1), the D_{H-C} parameter was optimized by fitting the CM5 charges on C-bonded hydrogen atoms in five molecules containing C–H bonds (namely, benzene, ethene, furan, pyrrole, and thiophene) to the corresponding ChEIPG charges (CHG)²⁷ by minimization of the following error function

$$\chi_1 = \sum_{I=1}^5 \sum_{J=1}^5 \sum_{k_H=1}^{N_J^H} (q_{IJK_H}^{CM5} - q_{IJK_H}^{CHG})^2 \quad (8)$$

where the CM5 charges are defined by eq 1 from the Hirshfeld charges, the index I indicates one of the five electronic structure methods (as listed above) used to calculate the corresponding ChEIPG and Hirshfeld charges at the molecular geometry optimized using the same method, the index J runs over the five molecules used in this step, and the index k_H runs over all N_J^H hydrogen atoms bonded to a carbon atom in the J th molecule. The D_{H-C} parameter was optimized while the remaining CM5 parameters (except for α) were set to zero. In this step, the parameter α was set to $1/0.353$ Å^{−1} ≈ 2.833 Å^{−1}. Note that the value of 0.353 Å was originally proposed by Pauling to describe C–C bonds.⁴⁴

In step 2, we optimized D_H , D_{He} , D_{Be} , D_B , D_N , D_O , D_F , D_{Na} , D_{Si} , and C with the fixed value of D_{H-C} obtained in step 1 and with $\alpha = 2.833$ Å^{−1} using eqs 5–7 over the whole training set of 614 compounds with reference dipole moments (see the next subsection for more details on the training set). We temporarily used eq 4 for any pair of elements, except for H–C. The following error function was minimized:

$$\chi_2 = \sum_{I=1}^5 \sum_{J=1}^{614} (\mu_{IJ}^{CM5} - \mu_J^{ref})^2 \quad (9)$$

where the CM5 charges are defined by eq 1 from the Hirshfeld charges, the index I indicates one of the five theoretical

methods used to calculate the corresponding Hirshfeld charges in the J th molecule at the molecular geometry optimized using the same method, μ_J^{ref} refers to the reference dipole moment of the J th molecule, and μ_{IJ}^{CM5} refers to the scalar dipole moment of the J th molecule obtained using the CM5 charges. The quantity μ_{IJ}^{CM5} is calculated by the equation

$$\mu = \sqrt{\sum_{Q=x,y,z} \left(\sum_{k=1}^N q_k Q_k \right)^2} \quad (10)$$

where we omitted the indices I and J for simplicity. In eq 10, the quantities x_k , y_k , and z_k are the Cartesian coordinates of atom k in the J th molecule optimized at the I th level of theory, q_k is the CM5 atomic charge (q_{IJK}^{CM5}) of atom k , and N is the total number of atoms in the J th molecule.

In step 3, we optimized only D_{H-N} , D_{H-O} , D_{C-N} , D_{C-O} , and D_{N-O} , now using eq 3 for the corresponding pairs of elements and using the parameters of step 1 and step 2 for all other mapping parameters. Finally, we repeated step 2 and step 3 at several values of α in order to optimize this parameter. Table 1 shows the final optimized values of D_H , D_{He} , D_{Be} , D_B , D_N , D_O , D_F , D_{Na} , D_{Si} , D_{H-C} , D_{H-N} , D_{H-O} , D_{C-N} , D_{C-O} , D_{N-O} , C , and α (i.e., 17 nonzero parameters). We also tested other optimization schemes (for example, by optimizing more independent parameters) which were found to be less favorable in terms of the overall efficacy of the final model. Note that the D_C parameter is determined by eq 6 using D_H and D_{H-C} , and the remaining atomwise parameters (D_{Ne} , D_{Al} , D_P , D_S , D_{Cl} , D_{Ar} , D_K , D_{Ge} , D_{As} , D_{Se} , D_{Br} , and D_I) are derived from the corresponding independent parameters (D_{He} , D_B , D_N , D_O , D_F , D_{Na} , and D_{Si}) using the optimized value of C and applying eq 7 recursively. See the values of these parameters in Table 1.

The CM5 model parameters were validated using the following cross-validation procedure. All of the 614 molecules were arranged as listed in the Supporting Information, and then every fifth molecule from that list was removed, thereby excluding 122 molecules. We repeated the CM5 optimization starting from step 2 based on the smaller training set of 492 molecules, and then we compared the CM5 atomic charges for

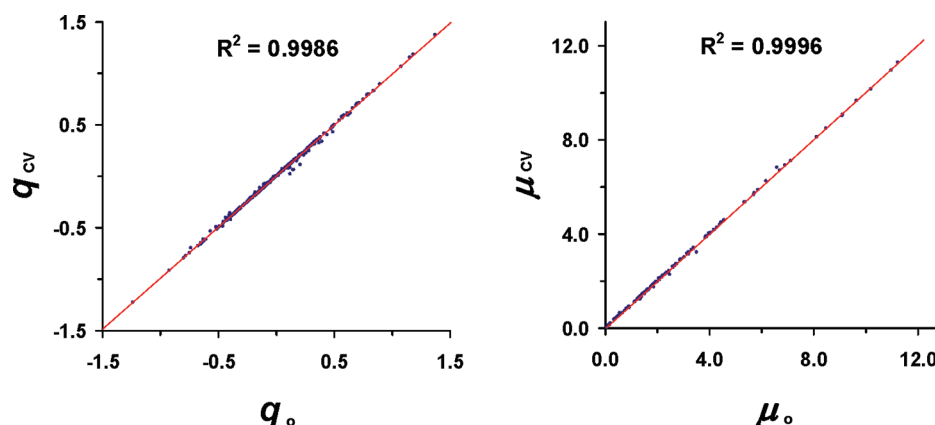


Figure 1. CM5 partial atomic charges (left) and CM5 dipole moments (right) calculated for 122 molecular structures excluded from the CM5 training set (614 data) within the cross-validation (cv) procedure described in section 2.2. The subscript “o” indicates that the corresponding CM5 charges (q) and dipole moments from those charges (μ , debyes) were calculated using the CM5 model parameters obtained over all 614 training data (Table 1). The subscript “cv” indicates that these charges and dipole moments were obtained using the CM5 parameters evaluated on the basis of the smaller training set of 492 data. The total number of individual atomic charges and dipole moments is 926 and 122, respectively. The R^2 value indicates the square of the correlation coefficient.

the excluded molecules obtained using the re-evaluated CM5 parameters to the corresponding charges obtained using the CM5 parameters optimized over the whole training set. The results of this cross-validation are shown in Figure 1. We observe that the overall accuracy of the CM5 model does not deteriorate substantially after exclusion of a reasonable number of data ($\sim 20\%$) from the optimization.

In addition, we have extended the CM5 model parametrized for 26 elements (namely, H–Ca, Zn, Ge–Br, and I) to the whole periodic table of elements assuming that $D_z = 0$ for Sc–Cu and recursively applying eq 7 to the rest of the elements which were not included in the CM5 parametrization. The extended set of CM5 parameters is given in the Supporting Information.

2.3. Training and Test Sets. The CM5 training set contains 614 molecular configurations for 614 unique molecules with either experimental reference dipole moments (388 data) taken from refs 58–67 or theoretical reference dipole moments (226 data). The latter are the density-based dipole moments averaged over the five theoretical methods (namely, M06-L/MG3S, M06/MG3S, M06-2X/MG3S, B3LYP/MG3S, and mPW1PW/MG3S) using molecular geometries optimized at the corresponding level of theory for each case.

We estimated the accuracy of the 226 theoretical reference dipole moments by calculating the error in the theoretical dipole moments evaluated as described above with respect to the 388 available experimental data, and we found that the mean signed deviation (theoretical minus experimental) over the 388 data is 0.07 D and the mean unsigned deviation is 0.13 D. Therefore, we believe that the 226 theoretical dipole moments should be almost as good as the corresponding experimental ones (which are not available for these molecules).

The CM5 training set includes a subset of 389 molecular configurations (with 319 experimental dipole moments and 70 theoretical dipole moments) used previously in the parametrization of CM4M as well as CM4 and CM3/MIDI!, and this part of the training set is described elsewhere.^{34,36–39} These data (CM4 subset) include only compounds composed of H, Li, C, N, O, F, Si, P, S, Cl, and/or Br. Note that the original

CM4 or CM4M training set³⁸ has 397 data, and it includes 16 theoretical dipole moments for eight unique amide molecules with two alternative conformations per each molecule (see ref 39 for details). In the present work, we consider for these molecules only (eight) global minimum molecular structures.

The CM5 training set contains 225 additional reference dipole moments for 225 unique compounds including 30 ions of the AW^+ , AXH^+ , AYH_2^+ , or AZH_3^+ type (where $A = \text{He, Ne, Ar; } W = \text{H, Li, F, Cl; } X = \text{O, S; } Y = \text{N, P; } Z = \text{C, Si}$), 12 zinc-containing ions, and six ions of the AW^+ type (where $A = \text{Be, Mg, Ca; } W = \text{F, Cl}$). For the ions, we use theoretical reference dipole moments calculated with respect to the center of nuclear charges. In addition to the 12 Zn ions, we also use six zinc-containing neutrals with theoretical reference dipole moments. The Zn subset (18 compounds) includes molecules and ions from previous work.⁶⁸ The CM5 training data also include 16 experimental dipole moments for 16 boron-containing molecules used previously.³⁵ A complete list of the 614 compounds in the CM5 training set is given in the Supporting Information along with the corresponding reference dipole moments.

We also tested 107 singly charged ions (51 cations and 56 anions) with nonzero reference dipole moments. These ions are taken from the Minnesota Solvation database.⁶⁹ For these ions, we used the reference density-based dipole moments averaged over the five theoretical methods listed above using the corresponding molecular geometries optimized by each method. These data were not used in the CM5 parametrization. A complete list of 107 test ions used in the present work is given in the Supporting Information along with the corresponding reference dipole moments. For ions, the dipole moment depends on the origin of the coordinate system, and we always use the center of nuclear charges.

2.4. Details of Computational Methods and Programs. In addition to Charge Model 5 (CM5), we also tested the performance of our earlier class IV charge models CM2, CM3, and CM4M and of population analysis methods including (in alphabetical order) atomic polar tensor-based (APT),¹⁷ Hirshfeld (HPA),^{1–3} Löwdin (LPA),^{13,14} Mulliken (MPA)¹² and minimum basis set Mulliken (MBS),^{70,71} and natural orbital (NPA)^{15,16} population analysis. In addition, we

considered ChElPG (CHG)²⁷ and Merz–Kollman–Singh (MKS) electrostatic potential schemes.^{24,25} The tested electronic structure methods include M06-L,^{45,46} M06,^{46,47} M06-2X,^{46,47} M06-HF,^{46,72} B3LYP,^{48–51} mPW1PW,⁵² Hartree–Fock theory (HF), and Austin Model 1 (AM1).⁷³

The AM1 calculations were performed using a locally modified version of the GAMESS program (GAMESSPLUS, version 2010–2).⁷⁴ The DFT and HF calculations of APT, HPA, LPA, MPA, MBS, NPA, CHG, and MKS atomic charges were carried out using Gaussian 09,⁷⁵ whereas the calculations of CM2, CM3, and CM4M charges were carried out using a locally modified version of Gaussian 09 (MN-GSM, version 2011). Note that a calculation of CMS charges does not require a modification of the Gaussian 09 code, and it is performed in the present work with an external script using the computed HPA charges from Gaussian 09's output file. This script is called CMSPAC and is freely available.⁷⁶

In the DFT and HF calculations, we tested various basis sets and effective core potentials (ECPs).^{77–79} All of the calculations labeled as MG3S in the present paper were performed using the MG3S basis set^{53–57} for all elements except for K, Ca, Zn, Ge–Br, and I (for which MG3S is not available). In these calculations, we used the core–valence triple- ζ (CVTZ) basis set for K and Ca,⁸⁰ the B2⁸¹ basis set with ECP-10⁸² for Zn, and the minimally augmented Karlsruhe basis set (ma-TZVP)^{83,84} for Ge–Br and I derived from the corresponding def2-TZVP basis sets⁸⁵ (with ECP-28⁸⁶ on I). Calculations labeled as ma-TZVP were performed using the ma-TZVP basis sets for all tested elements (with ECP-28 on I). Calculations labeled as DZVP and 3-21G were performed using the all-electron DZVP⁸⁷ and 3-21G⁸⁸ basis sets, respectively, for all tested elements including I. We also explored the 6-31G(d) basis⁸⁸ as implemented in Gaussian 09 (using the corresponding keyword) for all tested elements excluding I (in the calculations involving iodine-containing molecules in this case we used DZVP on all atoms). Further, in this article, we will sometimes use the A/B//A'/B' notation to show that the corresponding dipole moment is calculated at the A/B level of theory using the A'/B' optimized geometry (where A or A' refers to an electronic structure wave function level or density functional, and B or B' refers to a basis set). Note that A/B is the same as A/B//A/B.

We used the keyword *integral=ultrafine* in all calculations with Gaussian 09. The other settings were set by default including the values of intrinsic atomic radii used in the ESP calculation with an exception for CHG calculations involving K, Ca, Zn, Ge–Br, and I and for MKS calculations involving Ar, K, Ca, Ge–Se, and I when we used the values of van der Waals radii tabulated in refs 41 and 89 for these elements because the corresponding ESP radii are not defined by default.

The computed CMS partial atomic charges in several cases were also compared to the OPLS (Optimized Potentials for Liquid Simulations) charges from the OPLS_2005 force field used in the Macromodel utility,⁹⁰ as part of the Maestro computational package.⁹¹ The OPLS_2005 force field⁹² is an enhanced version of the OPLS all-atom force field of Jorgensen et al.⁹³

3. RESULTS

Tables 2 and 3 show mean unsigned (MUE) and mean signed (MSE) errors in the magnitudes of dipole moments calculated using CMS charges at the M06-L/MG3S, M06/MG3S, M06-2X/MG3S, B3LYP/MG3S, and mPW1PW/MG3S levels of

theory for different classes of tested compounds versus the corresponding errors in the magnitudes of density-based dipole moments and those calculated using APT, HPA, LPA, MPA, MBS, NPA, CHG, and MKS charges. The errors in the predicted dipole moments (μ) are computed as $\mu - \mu_{\text{ref}}$ with respect to the reference data (μ_{ref}). The latter are given in the Supporting Information. Table 4 shows mean unsigned errors in the dipole moments calculated using additional theoretical levels. Table 5 shows mean unsigned deviations in the partial atomic charges obtained by various methods using one small basis set and one large basis set, in this example, 6-31G(d) and MG3S, respectively.

4. DISCUSSION

To begin this section, we will discuss several novel features in the CMS algorithm in comparison with our previous class IV charge models, for example, CM4M as the most recent one. First of all, the CMS model employs Hirshfeld population analysis charges instead of those from Löwdin and redistributed Löwdin population analysis as used by the CM4M model. One reason for this change is that the HPA charges produce more accurate charge-based dipole moments in terms of MUEs over all classes of tested compounds when a larger basis set such as MG3S is employed (see Table 2). Another reason is that the values of HPA charges are less sensitive to the choice of basis set in general. Table 4 shows that the HPA-derived dipole moments are more accurate than those derived from LPA charges over 614 CMS data and over all 12 combinations of density functionals and basis sets tested in the present work, whereas the LPA-derived dipole moments are slightly more accurate over a test set of 107 ions only if a smaller basis set such as DZVP, 6-31G(d), or 3-21G is employed. However, the overall accuracy of the HPA-derived dipole moments remains low (MUE ~ 0.7 , Table 4) with respect to the accuracy of the corresponding density-based dipole moments. Table 3 indicates that the Hirshfeld population analysis usually predicts smaller values of μ in comparison with μ_{ref} , thereby systematically underestimating the polarity of tested molecules. However, Table 5 shows that the HPA charges are on average very insensitive to an extension of the basis set from 6-31G(d) to MG3S, while the LPA charges change very dramatically. Our tests indicate that the CMS mapping of HPA charges can provide more accurate dipole moments than those obtained by using the HPA charges alone, and at the same time it preserves the low basis set sensitivity of the HPA charges.

The CMS model employs the Pauling bond order that depends only on molecular geometry (see eq 2) instead of electronic-structure bond orders, for example, the Mayer bond order^{94–96} used in the earlier CMx models. This change greatly simplifies the mapping of class II charges without a loss of accuracy, making a CMS calculation less computationally demanding, and it should lead to a faster and more stable convergence of a self-consistent reaction field procedure within the generalized Born dielectric continuum approximation where the reaction field depends on the atomic charges (see ref 37 and references therein).

As described in section 2.2, the CMS parametrization involves a separate optimization of the $D_{\text{H-C}}$ parameter by fitting the CMS charges on hydrogen atoms in five molecules containing C–H bonds (benzene, ethene, furan, pyrrole, and thiophene) to the corresponding ChElPG charges, which is similar to the approach used in previous work.³³ According to Table 1, C–H bonds are found in 369 molecular structures out

Table 2. Mean Unsigned Errors in the Magnitudes of Dipole Moments (debyes) by Compound Class^a

class ^b	count	μ_{ref}^c	Den	mean unsigned error								
				population analysis						ESP		
				APT	HPA	LPA	MPA	MBS	NPA	CHG	MKS	CM5
HC	7	0.49	0.08	0.18	0.09	0.17	0.72	0.12	1.05	0.06	0.08	0.13
HNO	7	1.28	0.06	0.88	0.70	1.12	0.57	0.37	0.65	0.14	0.12	0.08
HCN	56	2.70	0.17	0.41	0.93	1.77	1.37	0.25	0.37	0.15	0.17	0.19
HCO	66	2.21	0.17	0.89	0.62	1.44	0.69	0.45	1.21	0.17	0.17	0.12
HCNO	24	3.34	0.14	1.10	0.88	1.89	0.56	0.50	1.14	0.13	0.14	0.16
He	10	1.46	0.05	0.59	0.42	0.81	0.32	0.23	0.26	0.11	0.10	0.19
Li	18	5.63	0.13	0.90	1.06	3.96	2.37	2.34	1.17	0.15	0.16	0.47
Be	16	3.58	0.07	0.79	1.14	3.43	2.46	1.69	1.03	0.18	0.22	0.37
B	16	2.12	0.15	1.03	0.54	1.13	0.76	0.54	0.70	0.15	0.15	0.19
F	45	1.86	0.11	1.90	0.58	1.21	1.33	0.96	1.55	0.12	0.11	0.13
Ne	10	3.26	0.11	1.23	0.70	0.94	0.55	0.26	0.26	0.14	0.14	0.36
Na	18	7.56	0.18	0.99	1.32	5.29	2.34	2.17	1.44	0.32	0.22	0.47
Mg	16	4.27	0.21	0.57	0.84	3.53	1.50	1.27	2.34	0.26	0.44	0.42
Al	12	2.62	0.08	1.42	1.00	1.67	1.37	1.04	2.97	0.21	0.60	0.65
Si	38	1.36	0.09	1.22	0.39	0.95	1.56	0.70	1.22	0.13	0.20	0.25
P	32	1.76	0.07	1.18	0.51	0.97	0.74	0.68	1.71	0.13	0.08	0.24
S	42	1.96	0.11	0.80	0.61	1.18	0.84	0.23	1.27	0.12	0.12	0.19
Cl	50	1.87	0.12	1.07	0.45	1.20	1.08	1.16	0.63	0.15	0.16	0.11
Ar	11	2.41	0.08	1.46	0.40	1.56	0.64	0.52	0.50	0.10	0.10	0.28
K	16	8.75	0.31	1.20	1.57	4.25	1.75	3.96	1.67	0.87	0.43	0.65
Ca	12	7.70	0.32	1.67	1.88	3.91	1.13	4.02	2.59	0.35	0.42	0.59
Zn	18	3.24	0.22	0.90	0.96	1.38	1.50	0.86	2.12	0.24	0.80	0.63
Ge	14	1.88	0.13	2.06	0.65	0.82	0.99	0.70	3.30	0.29	0.29	0.44
As	15	1.72	0.09	1.96	0.39	1.11	1.06	0.63	2.84	0.22	0.18	0.28
Se	17	1.21	0.11	1.66	0.48	0.91	0.97	0.72	1.88	0.17	0.21	0.24
Br	17	1.55	0.12	0.57	0.11	0.93	0.78	0.82	0.93	0.08	0.20	0.27
I	11	1.52	0.11	0.76	0.40	1.60	0.86	0.90	1.45	0.15	0.13	0.26
all above	614	2.71	0.14	1.07	0.70	1.71	1.15	0.91	1.31	0.18	0.20	0.26
CM4 data	389	2.21	0.13	1.01	0.62	1.41	1.08	0.68	1.07	0.14	0.15	0.18
ions	107	4.22	0.06	1.01	0.71	1.05	1.31	0.41	0.94	0.09	0.07	0.35

^aMean unsigned errors for each class were averaged over the five methods: M06-L/MG3S, M06/MG3S, M06-2X/MG3S, B3LYP/MG3S, and mPW1PW/MG3S. ^bA full list of compounds in each class is given in the Supporting Information. The HC data include compounds containing H and C and no other elements. The HNO data include compounds containing at most H, N, and/or O in any combination. The HCO data include compounds composed of H, C, and O. The HCNO data include compounds composed of H, C, N, and O. Other classes include compounds containing elements other than H, C, N, and O. The CM4 subset is part of the CM5 training set of 614 compounds. ^cReference dipole moments averaged over a given class.

of the 614 used in the CM5 parametrization. However, the value of $D_{\text{H-C}}$ does not correlate significantly with the magnitudes of the dipole moments of these molecules, making it difficult to optimize $D_{\text{H-C}}$ in any manner other than simply by fixing this parameter at some reasonable value before optimizing the remaining parameters. Table 6 shows partial atomic charges on hydrogen atoms in benzaldehyde, benzene, ethene, phenol, propane, and propene calculated by various methods in comparison with the corresponding OPLS force field charges.^{90–93} One should keep in mind though that the latter are designed for use in liquid-phase simulations when comparing them to the gas-phase charges, although the difference is expected to be small for most C–H bonds. The resulting CM5 charges are found to be consistent with the OPLS charges as well as with the charges obtained using earlier CMx models, which employed somewhat different strategies to determine the $D_{\text{H-C}}$ parameter. The ESP charges on H atoms in the CH₂ group of the propane molecule are negative, whereas those predicted by the other models in Table 6 are all positive, making it difficult to speculate which value for the charge on H is more “reasonable” in this molecule or in the

others. Nevertheless, Table 6 shows that the charges on H atoms bonded to carbon atoms are quite reasonable in the CM5 model.

The CM5 mean unsigned error in the magnitudes of dipole moments calculated using M06-L/MG3S, M06/MG3S, M06-2X/MG3S, B3LYP/MG3S, and mPW1PW/MG3S over the CM4 subset of 614 CM5 data is 0.18 D (Table 2), which is close to the typical MUE of the CM4M model obtained over 397 CM4M data used in the CM4M parametrization: 0.20 D for CM4M/M06-L/6-31G(d) and 0.24 D for CM4M/M06-L/6-31+G(d,p).³⁸ The MUE over the whole set of 614 data is slightly larger (0.26 D, Table 2). The CM5 mean signed errors are close to zero in many instances shown in Table 3. Table 2 shows that the CM5 model improves on the HPA method over 25 out of 27 compound classes within 614 CM5 data. The CM5 model is more accurate on average than other methods except for the CHG and MKS schemes, which yield charge-based dipole moments close to the density-based ones in many cases with a few exceptions (the K subset for CHG and the Al and Zn subsets for MKS). The CM5 model performs reasonably well over all studied classes of compounds except

Table 3. Mean Signed Errors in the Magnitudes of Dipole Moments (debyes) by Compound Class^a

class	count	μ_{ref}	Den	mean unsigned error								
				population analysis						ESP		
				APT	HPA	LPA	MPA	MBS	NPA	CHG	MKS	CM5
HC	7	0.49	0.08	0.04	0.05	0.15	0.61	0.05	0.96	0.02	0.07	0.07
HNO	7	1.28	0.05	0.05	−0.65	−1.01	−0.42	0.08	0.55	0.06	0.07	−0.04
HCN	56	2.70	0.12	−0.33	−0.91	−1.75	0.71	−0.21	0.10	0.06	0.10	0.03
HCO	66	2.21	0.11	0.80	−0.61	−1.39	0.41	0.41	1.18	0.10	0.11	0.02
HCNO	24	3.34	0.11	0.79	−0.88	−1.88	−0.30	0.45	1.14	0.09	0.11	−0.11
He	10	1.46	0.00	0.06	−0.23	−0.34	0.00	0.13	0.16	0.02	0.03	−0.03
Li	18	5.63	−0.06	0.81	−1.06	−3.96	−2.37	−2.34	1.06	−0.11	−0.08	−0.26
Be	16	3.58	0.00	−0.16	−1.13	−1.93	−1.59	−1.11	0.86	0.09	−0.09	−0.06
B	16	2.12	0.01	0.21	−0.54	−0.27	−0.59	0.17	0.34	0.02	0.01	−0.01
F	45	1.86	0.03	1.62	−0.57	−1.16	0.98	0.82	1.42	0.03	0.03	−0.08
Ne	10	3.26	0.00	1.23	−0.70	−0.93	−0.53	−0.18	0.22	−0.07	−0.08	−0.33
Na	18	7.56	−0.02	0.84	−1.32	−5.29	−2.33	−2.17	1.34	−0.27	−0.10	−0.18
Mg	16	4.27	0.08	−0.26	−0.74	−1.96	−0.28	−0.81	2.28	0.19	0.37	0.06
Al	12	2.62	0.00	0.89	−0.32	−0.98	1.32	0.28	2.85	0.18	0.56	−0.09
Si	38	1.36	0.02	1.14	−0.21	0.32	1.43	0.45	1.14	0.06	0.13	0.08
P	32	1.76	0.00	0.67	−0.30	−0.37	0.27	−0.16	1.54	−0.02	0.01	−0.07
S	42	1.96	0.07	−0.31	−0.60	−1.09	0.59	−0.01	−0.07	0.03	0.09	−0.01
Cl	50	1.87	0.05	0.92	−0.45	−1.09	0.71	1.01	0.29	0.10	0.11	−0.05
Ar	11	2.41	0.01	1.35	−0.34	−1.45	0.32	0.36	0.44	0.05	0.04	0.03
K	16	8.75	0.10	1.06	−1.55	−4.25	0.41	−3.02	1.64	−0.85	−0.35	−0.26
Ca	12	7.70	0.00	0.00	−1.81	−3.82	−0.43	−3.46	2.47	−0.04	−0.16	0.11
Zn	18	3.24	0.00	−0.77	−0.82	−0.33	−1.16	−0.68	2.11	−0.06	0.77	−0.08
Ge	14	1.88	0.07	2.05	0.12	0.42	0.77	−0.04	3.30	0.18	0.20	0.26
As	15	1.72	0.01	1.77	−0.08	0.94	0.90	−0.03	2.84	0.13	0.12	0.08
Se	17	1.21	0.05	1.19	−0.22	0.87	0.86	0.13	1.74	0.08	0.14	−0.04
Br	17	1.55	0.05	0.56	−0.02	0.24	−0.22	0.75	−0.27	0.01	0.14	0.13
I	11	1.52	0.03	0.29	−0.23	1.60	0.07	0.52	0.20	−0.04	0.06	0.00
all above	614	2.71	0.05	0.62	−0.61	−1.19	0.22	−0.10	1.04	0.02	0.09	−0.03
CM4 data	389	2.21	0.06	0.63	−0.58	−1.16	0.47	0.25	0.74	0.05	0.08	−0.02
ions	107	4.22	0.00	0.09	−0.69	−0.93	0.81	0.24	0.76	−0.05	−0.01	−0.29

^aMean signed errors for each class were averaged over the five methods: M06-L/MG3S, M06/MG3S, M06-2X/MG3S, B3LYP/MG3S, and mPW1PW/MG3S. See footnotes *b* and *c* of Table 2 for other details.

for Al- and Zn-containing compounds. However, the CM5 model outperforms any other charge method on these compounds except for the CHG scheme. The absolute CM5 errors are high for K- and Ca-containing compounds as well, but in these cases the reference dipole moments are among the largest on average, so the percentage errors are still reasonable. Concerning Al- and Zn-containing compounds, the MKS method also gives unexpectedly large errors (Table 2). This is apparently due to quite small values of the intrinsic atomic radii for Al (1.24 Å) and for Zn (1.00 Å) used in the MKS calculation with *Gaussian 09* by default. After repeating the MKS calculations with the values of van der Waals radii for Al (1.84 Å) and for Zn (2.01 Å) from ref 41, we can reduce the mean unsigned error over these compounds in the MKS dipole moments (Table 2) from 0.6 D to ~0.2 D. The performance of the CHG scheme on K-containing compounds can also be improved by optimizing the value of the intrinsic atomic radius for K.

The CM5 mean unsigned error over 614 data (Table 4) becomes relatively large when we use M06-HF or even larger when we use the HF method (MUE = 0.37 D, MSE = 0.20 D), which makes the tested molecules unrealistically polar, i.e., the CM5-derived dipole moment on average appears to be larger than the reference one in this case. However, this is not so much a problem with CM5 as it is a problem with HF.⁹⁷

The CM5 mean unsigned error in the M06-L calculations over 614 data remains nearly the same when we use more complete basis sets, e.g., 0.25 D with MG3S, 0.27 D with ma-TZVP, 0.28 D with DZVP, and 0.30 D with 6-31G(d). However, if we use the M06-L/3-21G method, then the corresponding MUE increases to 0.44 D. This is partly a problem with using 3-21G for geometry optimization because the error can be decreased to 0.36 D if one uses molecular geometries optimized with MG3S, i.e., with a larger basis set. Table 4 shows that at all tested levels of theory the CM5 model gives smaller averaged errors in the dipole moments over 614 data than the HPA method, predicting more accurate dipole moments (relative to the reference ones) in over 80% of cases when one uses M06-L, M06, M06-2X, B3LYP, and mPW1PW with the MG3S or ma-TZVP basis sets.

Now, we will discuss the performance of the CM5 model in predicting the dipole moments of 107 ions not used in the CM5 parametrization (Table 4). In comparison with the value of MUE = 0.25 D obtained over a set of 614 CM5 data (M06-L/MG3S), the absolute error averaged over 107 ionic data increases to 0.40 D. However, the average reference dipole moment for the ions is 4.22 D versus 2.71 D, as averaged over 614 CM5 data. Thus, we conclude that the relative error remains nearly the same between these two sets of data.

Table 4. Mean Unsigned Errors in the Magnitudes of Dipole Moments (debyes) by Level of Theory^a

class	Den	population analysis						ESP		CMS ^b
		APT	HPA	LPA	MPA	MBS	NPA	CHG	MKS	
M06-L/MG3S										
CM5 data	0.15	1.05	0.69	1.72	1.25	0.87	1.30	0.16	0.18	0.25 (82%)
test ions	0.11	0.92	0.76	1.09	1.53	0.36	0.86	0.15	0.12	0.40 (83%)
M06/MG3S										
CM5 data	0.13	1.10	0.69	1.71	1.13	0.91	1.32	0.18	0.18	0.25 (82%)
test ions	0.03	1.01	0.73	1.06	1.25	0.41	0.94	0.09	0.06	0.35 (86%)
M06-2X/MG3S										
CM5 data	0.14	1.10	0.69	1.70	1.09	0.93	1.35	0.19	0.23	0.27 (81%)
test ions	0.08	1.10	0.66	1.02	1.17	0.44	1.00	0.09	0.08	0.31 (86%)
M06-HF/MG3S										
CM5 data	0.29	1.20	0.68	1.67	1.26	1.02	1.40	0.33	0.38	0.33 (76%)
test ions	0.24	1.31	0.60	0.98	1.48	0.52	1.11	0.24	0.24	0.26 (88%)
B3LYP/MG3S										
CM5 data	0.14	1.06	0.73	1.71	1.13	0.94	1.27	0.20	0.23	0.27 (83%)
test ions	0.04	1.01	0.71	1.05	1.21	0.44	0.96	0.08	0.06	0.35 (85%)
mPW1PW/MG3S										
CM5 data	0.12	1.02	0.70	1.70	1.15	0.93	1.30	0.17	0.21	0.27 (83%)
test ions	0.03	0.99	0.70	1.05	1.40	0.43	0.95	0.06	0.04	0.33 (85%)
HF/MG3S										
CM5 data	0.39	1.39	0.60	1.64	1.22	0.98	1.52	0.38	0.44	0.37 (67%)
test ions	0.29	1.35	0.52	0.94	1.49	0.59	1.12	0.27	0.28	0.24 (71%)
M06-L/ma-TZVP										
CM5 data	0.17	1.06	0.70	1.07	0.86	0.86	1.23	0.18	0.21	0.27 (81%)
test ions	0.10	0.95	0.75	0.85	1.02	0.35	0.78	0.14	0.12	0.40 (84%)
M06-L/DZVP										
CM5 data	0.25	1.17	0.65	1.03	0.71	0.82	1.34	0.25	0.30	0.28 (76%)
test ions	0.19	0.97	0.70	0.54	0.56	0.34	0.91	0.20	0.19	0.38 (77%)
M06-L/6-31G(d)										
CM5 data	0.31	1.08	0.66	0.94	0.87		1.23	0.30	0.34	0.30 (75%)
test ions	0.36	0.97	0.76	0.43	0.62		0.80	0.36	0.35	0.44 (76%)
M06-L/3-21G										
CM5 data	0.60	1.20	0.74	1.04	1.26			0.60	0.63	0.44 (69%)
test ions	0.56	1.18	0.89	0.80	1.04		0.53	0.55	0.55	0.59 (74%)
M06-L/3-21G//M06-L/MG3S ^c										
CM5 data	0.49	1.07	0.78	1.10	1.24			0.50	0.53	0.36 (80%)
test ions	0.49	1.06	0.84	0.75	0.99		0.57	0.48	0.48	0.52 (72%)

^aThe CM5 set contains 614 data used for the CM5 parametrization. Note that only the first five theoretical levels given in this table were used for the CM5 parametrization. The test ions include a set of 107 singly charged ions with nonzero dipole moments not used for the CM5 parametrization with either level of theory. ^bThe number in parentheses indicates the percentage of data for a given class for which the CM5 model predicts more accurate dipole moments than the HPA method relative to the corresponding reference values. ^cThe corresponding dipole moment is calculated at the M06-L/3-21G level using the M06-L/MG3S optimized geometry.

The APT, LPA, MPA, MBS, and NPA charges yield less accurate dipole moments than those obtained with either the CM5 or HPA method, and the LPA and MPA methods are the least accurate methods to derive partial atomic charges in general (Table 2). Mean absolute deviations in the partial atomic charges obtained using basis sets of different size, for example, MG3S and 6-31G(d), are least significant in the case of CM5 and HPA, and they are most significant in the case of LPA and MPA (Table 5). Other methods (including NPA) exhibit a moderate basis set sensitivity. Figure 2 shows that CM5 atomic charges calculated using MG3S over 721 tested molecules change only a little from those calculated using a smaller basis set, 6-31G(d), as compared to the corresponding deviations in Löwdin charges. Figure 3 shows a similar trend when one compares CM5 charges calculated using 6-31G(d) and 3-21G, but in this case the corresponding deviations in Löwdin charges are much smaller than in the case of MG3S and

6-31G(d). Figure 4 shows that atomic charges obtained using the CM5 model are only slightly sensitive on average to the choice of density functional; in this example, they are less sensitive to the shift from M06-L/MG3S to M06-2X/MG3S than the corresponding CHG charges.

The basis set sensitivity of earlier class IV charge models cannot be evaluated in the same way as shown in Table 5 because those earlier models were not parametrized for basis sets larger than 6-31+G(d,p). The mean absolute deviation in the charges obtained at the CM4M/M06-L/6-31G(d) and CM4M/M06-L/6-31+G(d,p) levels over 397 neutral data from ref 38 is equal to 0.020.

Note that the correlation analysis of HPA charges computed over 721 tested molecules using M06-L/MG3S against the corresponding CHG charges yields $R^2 = 0.71$ (where R is the correlation coefficient), which is close to the value of $R^2 = 0.76$ obtained in ref 5 with the use of a smaller test set and HF/6-

311++G(d,p)//B3LYP/6-31G(d). The test set of 721 data used in the present work for testing the HPA method (as well as the CM5 model which is based on HPA charges) includes both neutral molecules and singly charged ions, even though the authors of ref 5 assert that HPA charges can be calculated unambiguously only for neutral molecules. The correlation analysis of HPA charges computed over 107 tested ions against the corresponding CHG charges yields $R^2 = 0.61$, which is smaller than the value of $R^2 = 0.71$ obtained over the whole set of 721 data. Nevertheless, we do not find any problem when one uses HPA for charged molecules, at least, in the way the HPA method is implemented in *Gaussian 09*.⁷⁵

Figures 5–10 and Tables 7–10 illustrate some applications of tested charge models. Table 7 gives partial atomic charges in the methyl acetate molecule as calculated by various methods. On the basis of the electronegativities of surrounding atoms, one can expect a qualitative trend that for the three carbon atoms in the molecule the C(1) charge should be most positive and the C(8) charge should be most negative. This is true in all of the cases except for LPA. However, individual charges

Table 5. Mean Unsigned Deviations in the Partial Atomic Charges Obtained Using One Small and One Large Basis Set^a

method	test set	
	614 CM5 data	107 test ions
APT	0.026	0.025
HPA	0.007	0.006
LPA	0.228	0.219
MPA	0.138	0.179
NPA	0.047	0.048
CHG	0.029	0.034
MKS	0.027	0.037
CM5	0.007	0.005

^aThe corresponding atomic charges calculated using M06-L/MG3S//M06-L/MG3S are compared to those calculated using M06-L/6-31G(d)//M06-L/6-31G(d). The deviations were averaged over 4536 atoms for the set of 614 CM5 data and over 1344 atoms for the set of 107 ions.

obtained using different algorithms remain quantitatively different by significant margins.

Figure 6 shows the dipole moment of the Ar...Cl van der Waals complex computed as a function of $R(\text{Ar}-\text{Cl})$. Values of the dipole moment calculated with any of the tested methods except for APT lie on nearly the same curve with the density-based dipole function, as one might expect. The APT dipole moment has a maximum at the equilibrium distance (3.13 Å), and the dipole moment vector changes its direction at $R(\text{Ar}-\text{Cl}) \approx 2.2$ Å.

Figure 7 shows that the ESP charges may depend on an internal bond rotation even in a simple molecule such as ethane, while the CM5 charges do not show such conformational dependence because they are not derived from the electrostatic potential.

Figure 8 shows CM5 atomic charges in several selected molecules. As expected from the electronegativities of the corresponding elements, the CM5 model predicts that the sodium atom has a small negative partial charge in the KNa molecule, and the sulfur atom has a small negative charge in the SSe molecule. Dipole moment values based on the CM5 atomic charges (in debyes, with available experimental reference values⁵⁸ given in parentheses) equal 2.97 (2.69) for KNa, 1.00 for SSe, 1.81 (1.85) for H₂O, and 1.55 (1.47) for NH₃.

Table 8 shows HPA, NPA, CHG, and CM5 excited-state partial atomic charges in the formaldehyde molecule calculated by *Gaussian 09* (with the *density=current* keyword) using time-dependent density functional theory (TDDFT)⁹⁸ with the M06 density functional and the MG3S basis set. We consider the ¹A₂ excited state of H₂CO; this corresponds to the lowest $n \rightarrow \pi^*$ transition. The dipole moment of formaldehyde decreases upon the $n \rightarrow \pi^*$ electronic excitation due to the transfer of some electron density from the oxygen atom to the carbon atom. The corresponding density-based dipole moment is 2.407 D in the ground state (the experimental value⁵⁸ is 2.332 ± 0.002 D) and 1.507 D in the excited state. All of the tested charge methods in Table 8 give a qualitatively correct prediction of this trend, but the CHG and CM5 charges are most accurate on an absolute basis, showing (as expected) that our parametrization does not break down for excited states.

Table 6. Partial Atomic Charges on Hydrogen Atoms in Selected Molecules^a

type of H	OPLS	AM1		HF/6-31G(d)		B3LYP/6-31G(d)		M06-L/6-31G(d)		M06-L/MG3S			
		LPA ^b	CM2	LPA	CM2	LPA	CM3	LPA	CM4M	HPA	CM5	CHG	MKS
ring	0.115	0.129	0.110	0.163	0.101	0.156	benzene 0.109	0.159	0.076	0.038	0.094	0.068	0.112
ring	0.115	0.137	0.120	0.173	0.112	0.165	benzaldehyde 0.118	0.167	0.085	0.043	0.100	0.082	0.120
CHO	0.000	0.078	0.062	0.127	0.066	0.115	0.068	0.107	0.026	0.024	0.086	−0.029	−0.038
ring	0.115	0.134	0.113	0.166	0.104	0.158	phenol 0.111	0.161	0.078	0.038	0.095	0.094	0.122
CH ₂	0.115	0.108	0.090	0.162	0.098	0.158	ethene 0.111	0.163	0.080	0.037	0.090	0.116	0.151
CH	0.115	0.113	0.095	0.151	0.088	0.147	propene 0.100	0.149	0.067	0.033	0.087	0.059	0.073
CH ₂	0.115	0.110	0.092	0.158	0.094	0.154	0.106	0.158	0.074	0.032	0.085	0.150	0.190
CH ₃	0.060	0.078	0.059	0.155	0.091	0.157	0.109	0.163	0.079	0.036	0.089	0.010	0.081
CH ₂	0.060	0.075	0.056	0.139	0.075	0.141	propane 0.094	0.144	0.061	0.025	0.080	−0.059	−0.052
CH ₃	0.060	0.069	0.050	0.146	0.081	0.148	0.099	0.152	0.068	0.027	0.078	0.038	0.064

^aAll calculations were carried out using the M06-L/MG3S optimized geometries. See section 2.4 for more details. ^bThe same as MPA for AM1.

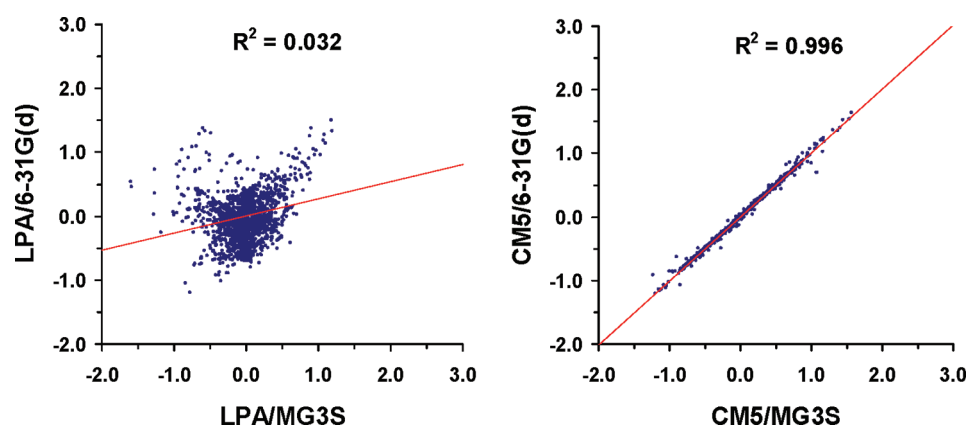


Figure 2. Partial atomic charges calculated using M06-L/MG3S versus those calculated using M06-L/6-31G(d) over 721 tested molecular structures (5880 charges) within Löwdin population analysis (left) and the CM5 model (right) where R is the correlation coefficient.

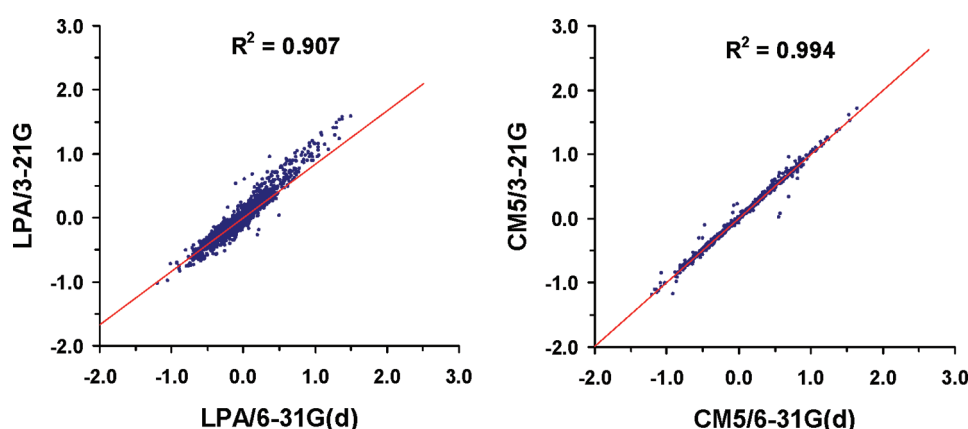


Figure 3. Partial atomic charges calculated using M06-L/6-31G(d) versus those calculated using M06-L/3-21G over 721 tested molecular structures (5880 charges) within Löwdin population analysis (left) and the CM5 model (right) where R is the correlation coefficient. The 3-21G calculations of atomic charges were carried out at the M06-L/MG3S geometry.

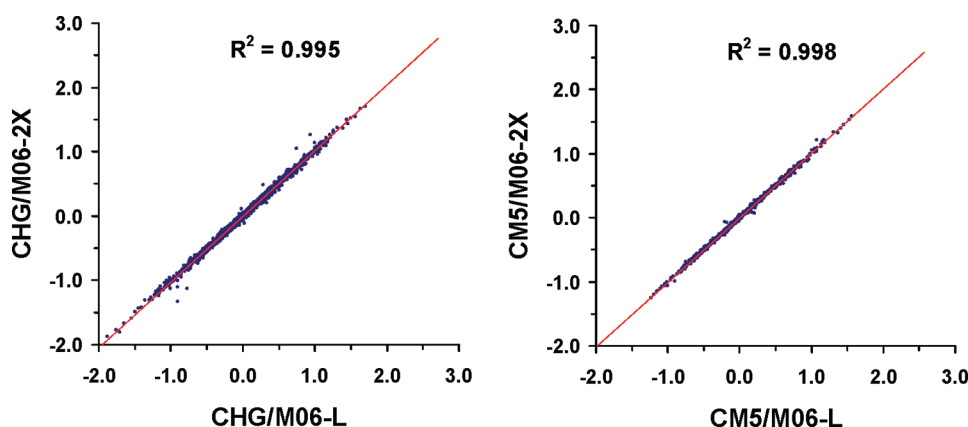


Figure 4. Partial atomic charges calculated using M06-L/MG3S versus those calculated using M06-2X/MG3S over 721 tested molecular structures (5880 charges) within the ChElPG scheme (left) and the CM5 model (right) where R is the correlation coefficient.

Table 9 shows HPA, NPA, CHG, and CM5 ground-state partial atomic charges in formaldehyde calculated by *Gaussian 09* (with the *density=current* keyword) using coupled cluster theory with single and double excitations (CCSD),^{99–101} as an example of calculating such charges with a post-HF correlated wave function calculation. In this calculation, we used the 6-311+G(2d,p) basis set, with no frozen molecular orbitals. The CCSD values of atomic

charges and the corresponding dipole moment of H_2CO in the ground state are close to those calculated by M06/MG3S (Table 8).

Table 10 compares dipole moments calculated from HPA, LPA, MPA, NPA, CHG, and CM5 atomic charges to the corresponding density-based dipole moments of 20 molecules containing several elements not presented in the CM5 training set (in particular Ti, Cr, Mn, Co, Ni, Cu, Y, Zr, Ru, La, Yb, Hf,

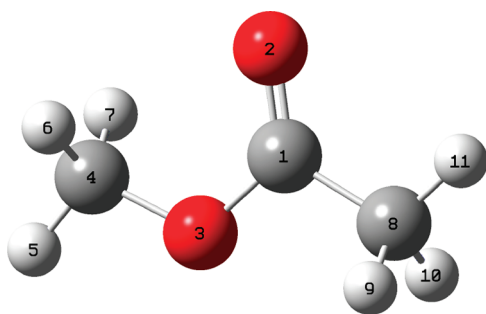


Figure 5. Numbering of atoms in methyl acetate. The partial atomic charges calculated at the M06-L/MG3S level of theory using various charge schemes are given in Table 7.

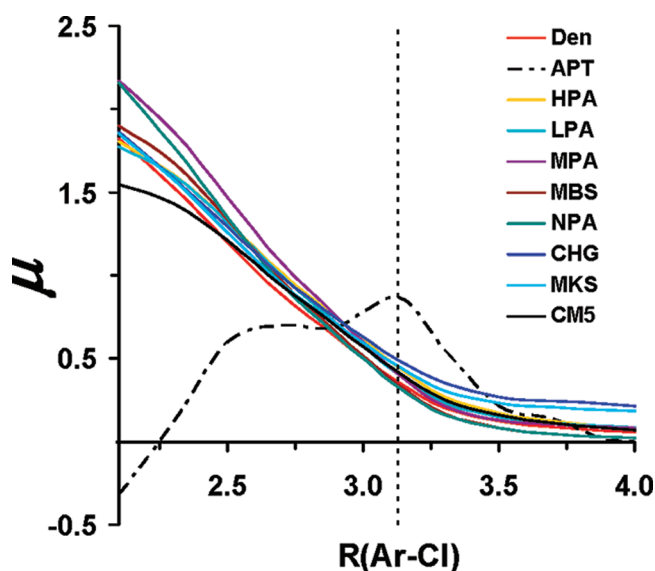


Figure 6. The dipole moment of $\text{Ar}\cdots\text{Cl}$ (μ , in debyes) calculated at various $\text{Ar}\cdots\text{Cl}$ distances (\AA). The dipole moment is based on the M06-L/MG3S electron density or on the corresponding atomic charges. The dashed vertical line corresponds to the $R_e(\text{Ar}\cdots\text{Cl})$ value.

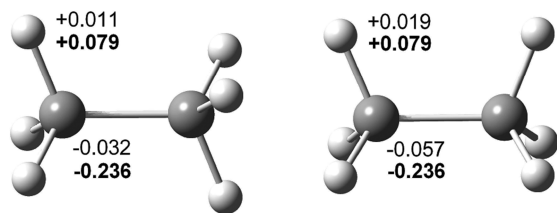


Figure 7. The MKS and CM5 partial atomic charges on H and C in the ethane molecule calculated at the M06-L/MG3S level for the global minimum structure (left) and for the saddle-point structure (right). The MKS values are in Roman font and the CM5 values are in bold.

Ta, Hg, and Pb). Available experimental dipole moments⁵⁸ are given as well. In these calculations (for both geometry optimization and dipole moment computations), we used the M06 density functional and the following basis sets and effective core potentials (ECPs): MG3S (all-electron basis) on H, N, O, F, and S; ma-TZVP (all-electron basis) on Ti, Cr, Mn, Co, Ni, and Cu; ECP-28 from refs 77 and 102 with the ma-TZVP valence-electron basis on Y, Zr, and Ru; ECP-28 with the corresponding valence basis from refs 103–105 on La and

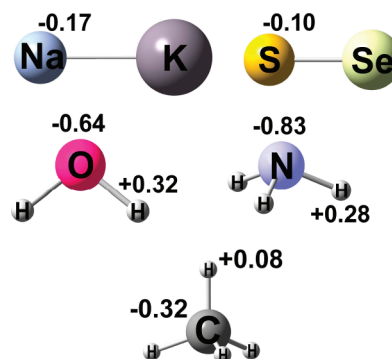


Figure 8. The CM5 partial atomic charges in KNa, SSe, H_2O , NH_3 , and CH_4 at the M06-L/MG3S level of theory. For comparison, the ChElPG charges are -0.05 (Na) in KNa, -0.10 (S) in SSe, -0.70 (O) in H_2O , -0.89 (N) in NH_3 , and -0.36 (C) in CH_4 .

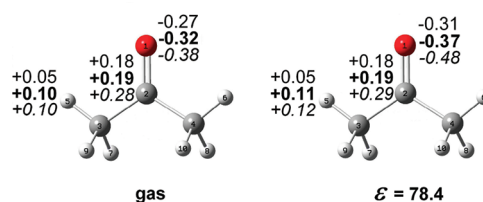


Figure 9. The HPA, CMS, and CM4M partial atomic charges in the acetone molecule in the gas phase and in water ($\epsilon = 78.4$). The HPA values are in Roman font, the CMS values are in bold, and the CM4M values are in italic. The charges on all hydrogen atoms are approximately the same in a given case. The charges on each of C(3) and C(4) (not shown) are -0.09 (HPA), -0.24 (CMS), and -0.25 (CM4M) in the gas phase and -0.09 (HPA), -0.23 (CMS), and -0.24 (CM4M) in solution. All calculations were carried out using M06-L/6-31+G(d,p) at the gas-phase M06-L/MG3S geometry.

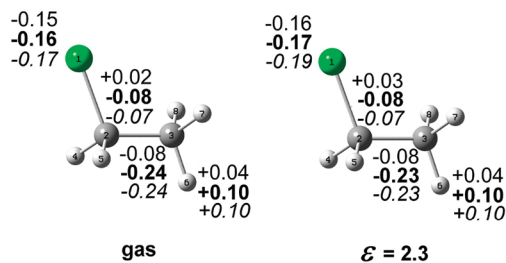


Figure 10. The HPA, CMS, and CM4M partial atomic charges in the ethyl chloride molecule in the gas phase and in tetrachloroethene ($\epsilon = 2.3$). The HPA values are in Roman font, the CMS values are in bold, and the CM4M values are in italic. The charges on H(4), H(5), H(7), and H(8) (not shown) are approximately the same as the charge on H(6) in a given case. All calculations were carried out using M06-L/6-31+G(d,p) at the gas-phase M06-L/MG3S geometry.

Yb (by using *Gaussian 09*'s keyword *mwb28*); ECP-60 from refs 77 and 102 with the ma-TZVP valence-electron basis on Hf, Ta, and Hg; and ECP-60 from refs 77 and 106 with the ma-TZVP valence-electron basis on Pb. The ma-TZVP basis sets were derived from the corresponding def2-TZVP basis sets^{77,85} according to a procedure described in ref 83. The corresponding partial atomic charges and Cartesian coordinates of these molecules are given in the Supporting Information.

Table 7. Partial Atomic Charges in the Methyl Acetate Molecule^a

atom	APT	HPA	LPA	MPA	MBS	NPA	CHG	MKS	CM5
C1	1.15	0.23	−0.51	0.35	0.52	0.83	0.86	0.90	0.27
O2	−0.71	−0.28	0.09	−0.38	−0.47	−0.61	−0.57	−0.57	−0.33
O3	−0.84	−0.13	0.19	−0.18	−0.38	−0.56	−0.42	−0.41	−0.22
C4	0.44	0.01	−0.02	−0.25	−0.08	−0.19	0.08	0.01	−0.12
H5	0.00	0.04	0.02	0.16	0.12	0.18	0.06	0.08	0.10
H6	−0.01	0.04	0.03	0.16	0.12	0.18	0.04	0.06	0.10
H7	−0.01	0.04	0.03	0.16	0.12	0.18	0.04	0.06	0.10
C8	−0.09	−0.08	0.05	−0.52	−0.29	−0.65	−0.51	−0.69	−0.22
H9	0.02	0.05	0.04	0.17	0.12	0.22	0.14	0.18	0.10
H10	0.02	0.05	0.04	0.17	0.12	0.22	0.14	0.18	0.10
H11	0.02	0.05	0.04	0.18	0.12	0.22	0.14	0.19	0.10

^aAll calculations were carried out using M06-L/MG3S. See Figure 5 and the text for more details.

Table 8. Ground- and Excited-State Partial Atomic Charges (q) and Dipole Moments (μ , in debyes) for the Formaldehyde Molecule^a

property	HPA		NPA		CHG		CM5	
	GS	ES	GS	ES	GS	ES	GS	ES
$q(\text{H})$	0.043	0.073	0.090	0.239	−0.029	0.178	0.100	0.131
$q(\text{C})$	0.148	−0.042	0.336	−0.209	0.506	−0.269	0.096	−0.094
$q(\text{O})$	−0.233	−0.104	−0.515	−0.269	−0.447	−0.087	−0.296	−0.167
μ	1.579	1.015	3.460	2.906	2.389	1.512	2.267	1.703

^aGS refers to the ground electronic state, and ES refers to the lowest $n \rightarrow \pi^*$ transition. Unless noted otherwise, we used TDDFT/M06/MG3S for the excited state and M06/MG3S for the ground state, with the M06/MG3S ground-state optimized geometry.

Table 9. CCSD/6-311+G(2d,p) Ground-State Partial Atomic Charges (q) and Dipole Moments (μ , in debyes) for the Formaldehyde Molecule^a

property	HPA	NPA	CHG	CM5
$q(\text{H})$	0.042	0.087	−0.014	0.100
$q(\text{C})$	0.137	0.316	0.457	0.085
$q(\text{O})$	−0.222	−0.490	−0.428	−0.285
μ	1.510	3.301	2.366	2.199

^aThese are the CM5 ground-state atomic charges and charge-based dipole moments calculated by CCSD/6-311+G(2d,p) using the M06/MG3S ground-state optimized geometry. The corresponding CCSD density-based dipole moment is 2.387 D.

Table 10 shows that the CM5 dipole moments are more accurate than the HPA dipole moments relative to the density-based dipole moments, as averaged over the 20 molecules containing transition metals and Pb, even in spite of the fact that we did not parametrize the model against a training set containing such elements. In general, the CM5 charges are more accurate than the corresponding HPA charges in molecules containing the corresponding metal in a higher (formal) oxidation state. For example, the CM5 dipole moments of ZrO_2 and HfO_2 are much more accurate (relative to either experimental reference values or theoretical density-based values) than the CM5 dipole moments of ZrO and HfO . The CM5 model performs poorly on LaO , but it quite accurately predicts the dipole moment of HLaO . In addition, the CM5 dipole moment of CuO is slightly more accurate than that of CuF . According to Table 10, the MPA dipole moments are as accurate as those calculated using the CM5 model. However, the MPA method does not perform well across a larger variety of chemical compounds (see Table 2). In general, the CM5 charges in the 20 molecules are closer to the

corresponding CHG charges (which give the most accurate dipole moments in Table 10) than the NPA charges. The latter tend to predict overly polar chemical bonds in these molecules.

Figure 9 shows the HPA, CM5, and CM4M partial atomic charges in the acetone molecule as calculated in the gas phase and in water using the dielectric continuum approach. In the latter case, the charges are calculated self-consistently within the generalized Born approximation with asymmetric descreening (GBAD) and the SM8AD values of intrinsic atomic Coulomb radii.¹⁰⁷ Dipole moment values based on the gas-phase charges for acetone equal 2.18 (HPA), 2.92 (CM5), and 3.23 (CM4M) D (the experimental reference⁵⁸ is 2.88 ± 0.03 D). Dipole moment values derived from the liquid-phase charges of acetone in water with the dielectric constant $\epsilon = 78.4$ are 2.68 (HPA), 3.60 (CM5), and 4.37 (CM4M) D, thereby increasing by 23% for HPA and CM5 and by 35% for CM4M, respectively. Values of the density-based dipole moment calculated using the corresponding liquid-phase wave function increase relative to the gas-phase one by 21 (HPA), 28 (CM5), and 30% (CM4M). Figure 10 shows the same set of charges for ethyl chloride in the gas phase and in tetrachloroethene ($\epsilon = 2.3$). In this case, the gas-phase dipole moments derived from HPA, CM5, and CM4M charges equal 1.63, 2.00, and 2.09 D, respectively (the experimental reference⁵⁸ is 2.05 ± 0.02 D). The liquid-phase dipole moments derived from HPA, CM5, and CM4M charges for ethyl chloride in tetrachloroethene are 1.76, 2.16, and 2.37 D, increasing by 8% (HPA and CM5) and 13% (CM4M). For comparison, the corresponding values of the density-based dipole moment increase by 7% (HPA) and 9% (CM5 and CM4M). The increase of the magnitudes of dipole moments in solution relative to those in the gas phase is similar to the results of previous work.^{108,109} This increase is typically larger if one uses CM4M. However, it is difficult to say how big this increase should be because the experimental

Table 10. Dipole Moments (debyes) of Selected Molecules Containing Elements Not Presented in the CM5 Training Set^a

molecule ^b	Den	HPA	LPA	MPA	NPA	CHG	CM5	reference
TiO	3.76	3.15	2.63	3.75	6.17	4.21	5.37	2.96 ± 0.05
CrO	4.80	3.07	3.34	5.19	5.98	4.81	4.45	3.88 ± 0.13
MnN ₂	4.35	1.55	1.83	4.75	3.72	4.04	4.25	N/A
CoNO	3.74	0.98	0.50	3.76	2.52	3.23	2.63	N/A
NiNO	2.78	1.12	0.52	2.77	3.36	2.59	2.33	N/A
CuO	4.65	2.38	2.81	3.08	5.94	4.50	3.26	4.5 ± 0.5
CuF	5.27	3.13	3.73	3.99	6.78	5.17	3.75	5.77 ± 0.29
YO	5.04	4.65	3.95	5.39	9.49	5.67	7.80	4.524 ± 0.007
ZrO	2.68	3.00	4.08	1.71	7.19	3.17	5.74	2.55 ± 0.01
ZrO ₂	8.08	4.68	4.21	6.05	9.08	8.17	7.57	7.80 ± 0.02
RuO ₂	1.73	0.82	1.09	2.39	1.88	1.63	1.47	N/A
LaO	4.06	3.05	2.93	5.75	9.69	4.57	7.88	3.207 ± 0.011
HLaO	6.84	3.15	3.32	5.69	9.27	6.91	7.34	N/A
YbF	4.41	4.00	4.60	6.25	8.61	5.05	5.44	3.91 ± 0.04
HfO	3.54	3.47	4.20	3.80	8.10	3.95	6.11	3.431 ± 0.005
HfO ₂	8.30	4.94	4.21	5.34	9.98	8.44	7.76	7.92 ± 0.01
TaN ₂	6.86	3.57	3.25	4.12	6.54	7.02	8.10	N/A
HgO	4.94	3.27	6.08	6.33	7.95	4.84	4.07	N/A
PbO	5.05	3.99	6.12	6.64	11.11	5.48	4.73	4.64 ± 0.50
PbS	4.19	3.94	5.63	7.09	9.02	4.63	4.44	3.59 ± 0.18
MUD ^c	0.00	1.69	1.89	1.21	2.58	0.30	1.21	0.47

^aCalculations were performed with M06 using basis sets and effective core potentials described in the text. The experimental reference dipole moments are given when available. N/A means not available. We considered the following spin multiplicities: quintuplet for CrO; triplet for TiO; doublet for MnN₂, NiNO, CuO, YO, LaO, YbF, and TaN₂; and singlet for all of the others. ^bSorted by the corresponding metal element's atomic number. ^cMean unsigned deviations calculated relative to the M06 density-based dipole moment values.

liquid-phase dipole moment is not even uniquely defined. Nevertheless, the molecular dipole moment in solution can be estimated with various theoretical models which can be useful for better understanding polarization effects in condensed phases.

To end this section, we will compare the CM5 model to the iterative Hirshfeld population analysis method (IHPA) proposed earlier.^{5,6} The IHPA method uses a Hirshfeld promolecule density determined self-consistently according to a procedure described in ref 5, and in contrast to the CM5 model, it improves on the original HPA method without using any empirical parametrization. Table 1 in ref 6 presents the IHPA partial atomic charges for 12 molecules calculated at the B3LYP/6-31++G(d,p)//B3LYP/6-31++G(d,p) level of theory. We compare these IHPA charges to the corresponding HPA and CM5 charges calculated in the present work at the same level of theory (see Table S4 in the Supporting Information). In general, the CM5 model predicts chemical bonds in the studied molecules that are more polar than those predicted by HPA and less polar than those predicted by the IHPA method. The CM5 dipole moments (MUE = 0.18 D) are considerably more accurate than either the HPA ones (MUE = 0.65 D) or the IHPA ones (MUE = 0.55 D) with respect to available experimental reference data.⁵⁸ The HPA dipole moments are systematically too small on average (MSE = −0.58 D), and the IHPA dipole moments are systematically too large (MSE = 0.41 D), whereas the CM5 dipole moments have a very small mean signed error (MSE = −0.04 D). Therefore, the CM5 model improves on the HPA method more dramatically than the IHPA approach does, at least, with respect to prediction of more accurate dipole moments over the tested molecules. In addition, since the CM5 model does not use any iterative steps, a CM5 calculation is less computationally demanding than an IHPA one, and thereby the CM5 method can be more readily

implemented for computations not only in the gas phase but also in condensed phases.

5. SUMMARY

We have presented a new algorithm to calculate partial atomic charges in an arbitrary molecule or ion in the ground or excited electronic state in gas and condensed phases, called Charge Model 5. The model is an improvement over all other charge methods tested in the present work over the total set of 721 reference data on dipole moments. The charges produced by the CM5 model should be of use for force field parametrization in molecular mechanics simulations, for computation of solvation free energies, and for generating realistic electrostatic potentials and multipole moments.

■ ASSOCIATED CONTENT

● Supporting Information

The CM5 model parameters extended to the whole periodic table and 721 reference data for tested molecules including reference and predicted dipole moments (part I), Cartesian coordinates (part II), and calculated partial atomic charges (part III). Part I also contains CM5, HPA, and iterative HPA partial atomic charges and dipole moments for 12 selected molecules from ref 6. This material is available free of charge via the Internet at <http://pubs.acs.org>

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Notes

The authors declare no competing financial interest.

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