A sort description of the methods used in ACC III

Empirical charge calculation methods

This section shortly describes the main idea of each method implemented in Atomic Charge Calculator III. Methods here are ordered according to the publication date.

For clarity, we use unifying naming scheme (which may differ from the one used in the original publication); the symbols used throughout the chapter: q_i stands for charge on ith atom, Q is the total molecular charge, N is the number of atoms in a molecule and $R_{i,j}$ represents the Euclidean distance between atoms i and j.

DelRe

Methods of Del Re [1] starts with the definition of a linear system in the form:

$$\delta_i = \delta_i^0 + \sum_j \gamma_{i,j}\delta_j \tag{1}$$

where j iterates over atoms bonded to i. δ_i^0 is an atom parameter, whereas $\gamma_{i,j}$ is a bond parameter. Solving for δ_i allow us to derive bond charges:

$$q_{i,j} = \frac{\delta_i - \delta_j}{2\epsilon_{i,j}} \tag{2}$$

where $\epsilon_{i,j}$ is another bond parameter. Finally, charge for each atom is computed as the sum of all involved bond charges.

PEOE

Partial equalization of orbital electronegativity [2, 3] is an iterative scheme in which the charges are moved along the bonds from the more electropositive atom to the more electronegative one. The amount of charge shifted is proportional to the difference of the electronegativities of the bonding partners. As effective electronegativity is defined here as a function of charge:

$$\chi_i^\alpha = A_i + B_i q^\alpha + C_i (q_i^\alpha)^2 \tag{3}$$

its value for each atom must be recomputed as it enters the next iteration.

The main idea of a charge transfer is expressed through the following equation:

$$q_i^\alpha = \left(\sum_j \frac{\chi_j^\alpha - \chi_i^\alpha}{D_i} + \sum_k \frac{\chi_i^\alpha - \chi_k^\alpha}{D_k} \right) \cdot \left(\frac{1}{2}\right)^\alpha \tag{4}$$

where j are atoms bonded to atom i with higher electronegativity and k are atoms bonded to atom i with lower electronegativity.

Since the generated charges produce an electrostatic field which further hinders the charge transfer, the dampening factor $(1/2)^\alpha$ was introduced to account for that fact. Usually, six iterations of 3 followed by 4 are necessary for charges to converge.

Finally, total atomic charge q_i is the sum of charge transfers across all the iterations:

$$q_i = \sum_\alpha q_i^\alpha \tag{5}$$

Charge2

Charge2 [4] is an iterative method in which charge increments from neighbor atoms are added to a central one.

$$q_i = q_i(\alpha) + q_i(\beta) + q_i(\gamma) \tag{6}$$

$$q_i(\alpha) = \sum_j \frac{\chi_j - \chi_i}{a} \tag{7}$$

$$q_i(\beta) = \sum_k \frac{(\chi_k - \chi_H)P_i}{b} \tag{8}$$

$$q_i(\gamma) = \sum_l \frac{(\chi_l - \chi_H)P_i}{bc} \tag{9}$$

$$\tag{10}$$

where

$$P_i = P_i^0 \left(1 + \alpha(q_i^0 - q_i)\right) \tag{11}$$

and j, k and l represents atoms one, two or three bonds apart from atom i, a, b, c and P^0 are atom parameters, q^0 is a formal charge, χ_H is an electronegativity of hydrogen, and α is a common parameter.

EEM

Contrary to the partial electronegativity equalization methods like PEOE or MPEOE, full electronegativity equalization is fundamental to the Mortier's Electronegativity Equalization Method [5].

According to the Sanderson's principle, the electronegativity of each atom gets equalized when atoms bond to form a molecule:

$$\overline{\chi} = \chi_1 = \ldots = \chi_N \tag{12}$$

The electronegativity of an atom in a molecule is expressed as:

$$\chi_i = A_i + B_i q_i + \sum_{i \neq j} \frac{q_j}{R_{i,j}} \tag{13}$$

where

$$A_i = \chi_i^0 + \Delta\chi_i \tag{14}$$

$$B_i = 2(\eta_i^0 + \Delta\eta_i) \tag{15}$$

χ^0 is an electronegativity of an isolated atom, η^0 is a hardness of an isolated atom. Δ symbols represent corrections for the molecular environment.

Finally, charge conservation principle holds:

$$Q = \sum_i q_i \tag{16}$$

Rewriting 13 for every atom in molecule subject to 12 and 16 yields a system of $N + 1$ linear equations:

$$\begin{bmatrix} B_1 & R_{1,2}^{-1} & \cdots & R_{1,N}^{-1} & 1 \\ R_{2,1}^{-1} & B_2 & \cdots & R_{2,N}^{-1} & 1 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ R_{N,1}^{-1} & R_{N,2}^{-1} & \cdots & B_N & 1 \\ 1 & 1 & \cdots & 1 & 0 \end{bmatrix} \cdot \begin{bmatrix} q_1 \\ q_2 \\ \vdots \\ q_N \\ -\overline{\chi} \end{bmatrix} = \begin{bmatrix} -A_1 \\ -A_2 \\ \vdots \\ -A_N \\ Q \end{bmatrix} \tag{17}$$

MPEOE

Modified Partial Equalization of Orbital Electronegativity [6] differs from original PEOE by expressing electronegativity as a linear function of charge, so that 3 is modified to:

$$\chi_i^\alpha = A_i + B_i q^\alpha \tag{18}$$

Other than that, the dampening factor $(1/2)^\alpha$ is a now considered as a bond type dependent parameter $f_{x,y}$ changing 4 to:

$$q_i^\alpha = \sum_j \frac{\chi_j^\alpha - \chi_i^\alpha}{D_i} f_{i,j}^\alpha + \sum_k \frac{\chi_i^\alpha - \chi_k^\alpha}{D_k} f_{i,k}^\alpha \tag{19}$$

QEq

Charge Equilibration (QEq) [7] is similar to EEM. However, originally, it was meant as an iterative scheme as parameter $J_{i,i}$ for hydrogen was defined to be charge-dependent.

$$\chi_i = \chi_i^0 + J_{i,i}^0 q_i + \sum_{i \neq j} J_{i,j} q_j \tag{20}$$

In the original publication values for the Coulomb repulsion term $J_{i,j}$ were obtained using *ab-initio* calculations. To simplify the process, several empirical terms were developed to substitute $J_{i,j}$ with some simple expression.

The system of linear equations is constructed and solved for q similarly to the one in EEM.

ABEEM

Atom-bond Electronegativity Equalization Method [8] extends original EEM to also include bond electronegativities into the equalization scheme. Electronegativity of atom i is expressed as:

$$\chi_i = A_i + B_i q_i + C_i \sum_{i-j} q_{i-j} + k \sum_{i \neq j} \frac{q_j}{R_{i,j}} + k \sum_{k-l \neq i-j} \frac{q_{k-l}}{R_{i,k-l}} \tag{21}$$

where A, B and C are atom parameters, k is a common parameter, q_{i-j} denotes the charge on the bond $i-j$. Distance to a bond is computed to its center proportional to the covalent radius of the constituent atoms. Electronegativity of a bond $i-j$ has the following form:

$$\chi_{i-j} = A_{i-j} + B_{i-j} q_{i-j} + C_{i-j,i} q_i + D_{i-j,j} q_j + k \sum_{k \neq i,j} \frac{q_k}{R_{i-j,k}} + k \sum_{k-l \neq i-j} \frac{q_{k-l}}{R_{i-j,k-l}} \tag{22}$$

where A, B, C and D are bond parameters and k is a common parameter.

Solving the system of linear equations provides us with the atomic and bond charges. The bond charges are then added onto the constituent atoms proportionally to their covalent radii yielding the final atomic charges.

GDAC

Further modification of MPEOE method is coined Geometry-dependent Atomic Charges [9]. GDAC modifies the dampening term $f_{x,y}$ to be geometry dependent:

$$f_{x,y} = 1 - \frac{R_{x,y}}{R_x^{vdw} + R_y^{vdw}} \tag{23}$$

where R_x^{vdw} stands for the van der Waals radius of atom x.

MGC

Molecular Graph Charge model (MGC) [10, 11] uses molecular graph representation of the molecule as it is inspired by electrical circuits and Kirchhoff's current laws. Therefore, no atomic coordinates are employed.

MGC constructs auxiliary matrix $\boldsymbol{S}$ in the following way:

$$\boldsymbol{S} = -\boldsymbol{A} + \boldsymbol{D} + \boldsymbol{I} \tag{24}$$

where $\boldsymbol{A}$ is a connectivity matrix, $\boldsymbol{D}$ represents diagonal degree matrix and $\boldsymbol{I}$ is a standard identity matrix.

Equalized electronegativities are obtained from those of isolated atoms as a solution to the system of linear equations.

$$\boldsymbol{S}\boldsymbol{\chi} = \boldsymbol{\chi}^0 \tag{25}$$

Finally, partial atomic charges are computed as a difference between equalized and standard electronegativities of respective atoms, divided by the average electronegativity χ_M (geometric average).

$$\boldsymbol{q} = \frac{\boldsymbol{\chi} - \boldsymbol{\chi}^0}{\boldsymbol{\chi}_M} \tag{26}$$

SFKEEM

Selfconsistent Functional Kernel Equalized Electronegativity Method [12] develops on EEM's main idea. However, it incorporates different hardness matrix. The electronegativity equalization principle in SFKEEM is expressed as:

$$\chi_i = A + 2B_i q_i + \sum_{i \neq j} 2\sqrt{B_i B_j}\,\mathrm{sech}(\sigma R_{i,j}) \tag{27}$$

where A, B and σ are empirical parameters and sech is a hyperbolic secant function.

KCM

Kirchhoff Charge Model [13] builds a Laplacian matrix $\boldsymbol{L}$ as:

$$\boldsymbol{L} = \boldsymbol{B}^T \boldsymbol{W} \boldsymbol{B} \tag{28}$$

where $\boldsymbol{B}$ is an incidence matrix and $\boldsymbol{W}$ is a diagonal "softness" matrix with elements $w_{i,i} = 1/(\eta_i + \eta_j)$, where η stands for hardness of an atom.

Atomic charges are derived using the following expression:

$$\boldsymbol{q} = (\boldsymbol{L}^{-1} - \boldsymbol{I})\boldsymbol{\chi}^o \tag{29}$$

where $\boldsymbol{L}^{-1}$ is an inverse of $\boldsymbol{L}$ and $\boldsymbol{\chi}^o$ represents a vector of electronegativities of isolated atoms.

DENR

Dynamic electronegativity relaxation [14] is an iterative 2D scheme in which charges are derived using a Laplacian matrix:

$$\boldsymbol{q}^{(n+1)} = (\boldsymbol{I} + c\Delta t \cdot \boldsymbol{B}_0)^{-1} \cdot (\boldsymbol{q}^{(n)} - c\Delta t \cdot \boldsymbol{a}_0) \tag{30}$$

where $\boldsymbol{B}_0 = \boldsymbol{L}\boldsymbol{\eta}_0$ and $\boldsymbol{a}_0 = \boldsymbol{L}\boldsymbol{\chi}_0$. Note that $\boldsymbol{\eta}_0$ is a diagonal matrix of atomic hardnesses.

TSEF

Topologically Symmetrical Energy Function [14] has electronegativity equalization principle as its base but changes off-diagonal term to include bond distance rather than Euclidean distance making TSEF conformationally independent.

$$\phi_{i,j} = \alpha \cdot K(MDP_{i,j}) \cdot \frac{1}{0.84 \cdot MDP_{i,j} + 0.46} \tag{31}$$

where MDP stands for *minimal distance path*, i.e., minimal number of bonds between two atoms, K is parameter and α is a unit conversion factor.

SMP/QEq

Self-Consistent Charge Equilibration Method [15] builds upon the idea of the original QEq, electronegativity of an atom is formalized as a function of charge, thus the whole scheme is a iterative one. The main equation follows:

$$\chi_i(q_i) = A_i + 2\lambda(q_i)q_i + \sum_{i \neq j} J_{i,j} q_j \tag{32}$$

where

$$\lambda(q_i) = B_i + C_i q_i + D_i (q_i)^2 \tag{33}$$

and

$$J_{i,j} = \left(\frac{1}{(2\sqrt{B_i B_j})^3} + R_{i,j}^3 \right)^{-1/3} \tag{34}$$

where A, B, C and D are atom parameters.

VEEM

Valence electrons equilibration method [16] calculates atomic charges based on the number of valence electrons of individual atoms and atomic groups.

First, equalized electronegativity is calculated for the whole molecule:

$$\chi_{ve} = \frac{\sum_i \chi_i N_{ve,i}}{\sum_i N_{ve,i}} \tag{35}$$

where χ_i is an electronegativity of isolated atom i; $N_{ve,i}$ stands for the number of valence electrons of atom i.

Finally, the partial atomic charge of atom i is computed as:

$$q_i = N_{ve,i} \frac{\chi_{ve} - \chi_i}{\chi_{ve}} \tag{36}$$

EQeq

Extended charge equilibration method [17] builds upon original QEq scheme, which is modified to take the following form (the simplest, non-periodic case without different charge centers):

$$\chi_i = \chi_i^0 + J_i^0 q_i + \frac{K}{2} \sum_{i \neq j} q_j \left(\frac{1}{R_{i,j}} + O_{i,j} \right) \tag{37}$$

where

$$\chi_i^0 = \frac{IP_i + EA_i}{2} \tag{38}$$

$$J_i^0 = IP_i - EA_i \tag{39}$$

K is a constant; IP and EA stand for ionization potential and electron affinity, respectively, and

$$O_{i,j} = \exp\left(-\frac{J_{i,j}^2 R_{i,j}^2}{K^2}\right) \cdot \left(\frac{J_{i,j}}{K} - \frac{J_{i,j}^2 R_{i,j}}{K^2} - \frac{1}{R_{i,j}}\right) \tag{40}$$

where $J_{i,j}$ is a geometric mean of J_i^0 and J_j^0.

EQeq+C

Bond-order-corrected Extended Charge Equilibration Method [18] follows exactly the same procedure as EQeq, however, after the computation is done, some corrections are added to the original charges, i.e.:

$$q_i = q_i^0 + \sum_{j \neq i} T_{i,j} B_{i,j} \tag{41}$$

where q_i^0 is original charge from EQeq, and

$$T_{i,j} = D_i - D_j \tag{42}$$

$$B_{i,j} = \exp\left[-\alpha\left(R_{i,j} - r_i - r_j\right)\right] \tag{43}$$

where D is an atom parameter, α is a common parameter and r stands for covalent radius.

SQE

Split-charge Equilibrium method [19] is based on the electronegativity equalization principle. However, unlike EEM or QEq, it does not perform equalization on a level of individual atoms but switches the problem to a bond domain by defining *split-charges*, i.e., charges located on the bonds. The final atomic charge as a sum of the split-charges of the bonds that a particular atom forms. Formally, the atomic charge on atom i is expressed as:

$$q_i = \sum_{j \in BA(i)} p_{i,j} \tag{44}$$

where $BA(i)$ is a set of atoms bonded to atom i, and $p_{i,j}$ is a split-charge on the bond $i - j$.
SQE method written in the form of the system of linear equations is described by Equation 45:

$$\left(THT^T + \mathrm{diag}(\kappa)\right) q_{sp} = T\chi \tag{45}$$

where q_{sp} is a vector of split-charges, T is an incidence matrix describing the molecular topology, $\mathrm{diag}(\kappa)$ is a diagonal matrix with bond hardnesses, χ is a vector of atomic electronegativities, and H is a hardness matrix that describes the interactions between the atoms.

To reconstruct the atomic charges q from the split-charges, the following transformation is made:

$$q = T^T q_{sp} \tag{46}$$

SQE+q0

SQE+q0 [20], an extension to SQE, adds formal charges to work as initial seeds for the computation of partial atomic charges which might help in molecules that contain charged functional groups. This change is expressed in Equations 47 and 48:

$$\left(THT^T + \mathrm{diag}(\kappa)\right) q_{sp} = T(\chi - Hq_0 + \eta * q_0) \tag{47}$$

where q_0 is a vector of initial formal charges, η is a vector of atomic hardnesses (i.e., $J_{i,i}$ terms), and $*$ is an element-wise product. Equation 46 is then trivially modified to:

$$q = T^T q_{sp} + q_0 \tag{48}$$

SQE+qp

SQE+qp [21] replaces the formal charges q_0 with the parameterized ones q_p. To preserve the total charge of the molecule, these parameterized values must be normalized first:

$$q_{pn} = q_p - \frac{1}{N}\left(1^T q_p - Q\right) \tag{49}$$

$$\tag{50}$$

where 1^T is a row vector of ones and N is the number of atoms in a molecule. The rest of the procedure is analogous as in SQE+q0:

$$\left(THT^T + \mathrm{diag}(\kappa)\right) q_{sp} = T(\chi - Hq_{pn} + \eta * q_{pn}) \tag{51}$$

$$q = T^T q_{sp} + q_{pn} \tag{52}$$

Complexity of implemented methods

The following table summarizes computational costs of the implemented methods, both in terms of time and memory complexity (expressed using $\mathcal{O}$ notation). The symbol N denotes the number of atoms, M is the number of bonds. Methods are grouped according to whether they depend on molecular geometry (3D) or not (2D).

2D methods (topology-based)			
Method	Time	Memory	Suitable for large systems
DelRe	N^3	N^2	no
PEOE	$N + M$	N	yes
Charge2	$N + M$	1	yes
MPEOE	$N + M$	N	yes
MGC	N^3	N^2	no
DENR	N^3	N^2	no
KCM	N^3	N^2	no
TSEF	N^3	N^2	yes
VEEM	N	1	yes
3D methods (geometry-dependent)			
Method	Time	Memory	Suitable for large systems
GDAC	$N + M$	N	yes
EEM	N^3	N^2	yes*
QEq	N^3	N^2	yes*
SMP/QEq	N^3	N^2	yes*
SFKEEM	N^3	N^2	yes*
EQeq	N^3	N^2	yes*
EQeq+C	N^3	N^2	yes*
ABEEM	$(N + M)^3$	$(N + M)^2$	no
SQE	M^3	M^2	no
SQE+q0	M^3	M^2	no
SQE+qp	M^3	M^2	no

In addition to asymptotic complexity, practical applicability depends on the availability of complexity-reduction techniques. Methods marked with * support cutoff and cover schemes, which significantly reduce computational cost and memory usage for large systems (see the details in the next section). Methods without these techniques (e.g., SQE and related variants) exhibit unfavourable scaling and are therefore not recommended for large molecules ($N > 20000$ atoms). This classification is reflected in ACC III, where such methods are excluded from default selection for large systems. However, when using ChargeFW2 locally, users may override this behaviour if needed.

Illustrative performance benchmarks

To complement the asymptotic complexity analysis, we provide *illustrative* benchmark measurements for selected methods (PEOE, EEM, and SQE+qp). All measurements were performed on a single CPU core of an AMD Ryzen 7 9700X processor with 64 GB RAM, Fedora 43, using the CLI ChargeFW2 application. Reported runtimes correspond to wall-clock time.

System	Method	Atoms	Time (s)	Memory	Unit	Note
Small molecule	PEOE	17	< 0.01	7	MB	–
	EEM	17	< 0.01	6	MB	–
	SQE+qp	17	< 0.01	7	MB	–
Protein	PEOE	5761	0.02	18	MB	–
	EEM	5761	1.4	530	MB	–
	SQE+qp	5761	7.1	1055	MB	–
Large protein	PEOE	40738	0.16	97	MB	–
	EEM	40738	36.2	98	MB	Cutoff used*
	SQE+qp	40738	391.7	36.7	GB	**

* For supported methods (see the table), cutoff is automatically used for molecules having more than 20000 atoms.

** This option is not considered suitable for such a molecule by default, and therefore not listed on the ACC III web site. It has to be selected manually, when using ChargeFW2 locally.

Assessment of charges quality

In order to compare two sets of charges, two descriptors are commonly used. The first one is the Pearson's correlation coefficient (R); the second one is the root mean square deviation (RMSD). In the following sections, we denote the charge sets as $X = (x_1, \ldots, x_n)$ and $Y = (y_1, \ldots, y_n)$, $\overline{x}$ and $\overline{y}$ represent the arithmetic means of x_i and y_i values, respectively.

Pearson's correlation coefficient (R)

Pearson's correlation coefficient describes the linear dependence between two sets of values. Its value ranges from -1 (negative correlation) through 0 (no correlation) to 1 (positive correlation). Sometimes, the value of squared Pearson's correlation coefficient (R^2) is used.

$$R(X,Y) = \frac{\sum_{i=1}^{n}(x_i - \overline{x}) \cdot (y_i - \overline{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \overline{x})^2} \cdot \sqrt{\sum_{i=1}^{n}(y_i - \overline{y})^2}}$$

Root mean square deviation (RMSD)

Root mean square deviation is another measure which can be used to compare two sets of values. When RMSD is zero, the sets are identical. Otherwise, a smaller value indicates higher similarity.

$$RMSD(X,Y) = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(x_i - y_i)^2}$$

Cutoff and cover approaches

Solving the electronegativity equalization system of linear equations can be troublesome for very large structures as it requires, in general, $\mathcal{O}(N^3)$ steps and $\mathcal{O}(N^2)$ memory. The original AtomicChargeCalculator (ACC) introduced two *divide and conquer* complexity reduction algorithms to overcome this issue. Since ACC only supports EEM, these approaches were called *EEM Cutoff* and *EEM Cover*. ACC III extended these approaches to other applicable methods, referencing them simply as *cutoff* and *cover*.

Here, we provide the description of these approaches as stated in the ACC publication's [22] Additional file 1:

EEM Cutoff

For each atom in the molecule, ACC generates a fragment made up of all atoms within a cutoff radius R of the original atom. The values of the inter-atomic distances and EEM parameters are obtained in the same way as when solving the full EEM matrix. The total fragment charge Q_F is a quota of the total molecular charge Q, proportional to the number of atoms in the fragment (N_F), and irrespective of the nature of these atoms:

$$Q_F = \frac{Q \cdot N_F}{N}$$

Then ACC solves the EEM matrix equation for this fragment, and returns the charge for the atom used when generating the fragment. The same procedure is applied for all fragments, obtaining a set of charges for all the atoms in the molecule. Then, each atomic charge q_i is corrected by the addition of:

$$\frac{Q - \sum_{i=1}^{N} q_i}{N}$$

so that the sum of all atomic charges equals the total molecular charge Q.

EEM Cover

The EEM Cover approach builds on the principles of EEM Cutoff to split the EEM matrix into smaller matrices. However, EEM Cover generates fragments only for a subset of atoms in the molecule. The procedure selects fragment-generating atoms so that: (i) no two such atoms are connected to each other, and (ii) each atom in the molecule has at least one neighbor (within two bonds) which was selected. This procedure ensures that each atom in the molecule will eventually contribute to at least one fragment, and thus the entire volume of the molecule is covered. ACC solves the EEM matrix equation for each fragment, and returns a list of charge contributions for all atoms encountered in the calculations. The charge on each atom in the molecule is then computed as the sum of its charge contributions from all fragments where the atom is present. Further, each atomic charge q_i is corrected by the addition of:

$$\frac{Q - \sum_{i=1}^{N} q_i}{N}$$

so that the sum of all atomic charges equals the total molecular charge Q.

Time and space complexity

For a given sphere radius R, these approaches effectively reduce the time and space complexity to $\mathcal{O}(R^6N + R^2N\log N)$ and $\mathcal{O}(R^4N + N\log N)$, respectively. [22]

Accuracy

Employing these approximative schemes may introduce some loss of accuracy when comparing with the original charges. Their assessment was made for original ACC for EEM [22] or in [23] where author states that "according to tests, the EEM Cover method produces results that are practically identical to solving the EEM matrix for the full original system". Here, we present a simplified[1] version of the table taken from [23]:

PDB ID	# of atoms	Total charge	R	RMSD
1lfg	5884	0	0.9998	0.0080
		-10	0.9999	0.0064
		8	0.9997	0.0094
35tu	13934	0	0.9999	0.0039
		-10	1.0000	0.0034
		8	0.9999	0.0045
1tye	21013	0	1.0000	0.0033
		-10	1.0000	0.0030
		8	0.9999	0.0037
1aoc	28708	0	1.0000	0.0021
		-10	1.0000	0.0019
		8	1.0000	0.0024

Table 1: Comparison of Full EEM vs. EEM Cover method for computing partial atomic charges. Parameters EX-NPA_6-31Gd_gas [24] were used in the computation.

[1] Only for $R = 12$ Å, which is used in ACC III.

Notes on the implementation

Following section presents some notes and discusses differences in implementation of the some methods compared to the description used in original publication.

GDAC

Only a subset of the parameters is used.

QEq

The scheme is not iterative, expression for $J_{i,j}$ is taken from [25] as in SMP/QEq:

$$J_{i,j} = \left(\frac{1}{(2\sqrt{B_i B_j})^3} + R_{i,j}^3 \right)^{-1/3} \tag{53}$$

EQeq and EQeq+C

Only the non-periodic case without non-zero charge centers is supported.

SQE, SQE+q0, SQE+qp

The off-diagonal term in the hardness matrix has the form following form taken from [26]:

$$J_{i,j} = \frac{\mathrm{erf}\left(R_{i,j} (2w_i^2 + 2w_j^2)^{-1/2} \right)}{R_{i,j}} \tag{54}$$

Applications of charges

Partial atomic charges, obtained by empirical charge calculation methods, can be applied for example in the following fields:

- descriptors for QSAR and QSPR modelling [27, 28, 29, 30, 31, 32, 33, 34, 35]
- pharmacophore design [36, 37, 38]
- virtual screening [39, 40, 41]
- molecular docking [42, 43, 44]
- similarity searches [45, 46, 47]
- conformers generation [48]
- molecular dynamics [7, 49, 50, 51]
- study of mechanisms of chemical actions [52, 44, 53]

Overview of parameter sets

The following table summarises the parameter sets available in Atomic Charge Calculator III. The name is a clickable link to the publication where the parameter set was introduced. The *Coverage* column indicates the chemical elements to which each parameter set applies. The symbol * denotes parameter sets with additional restrictions on atom environments (typically related to the highest bond order), while + indicates parameter sets with additional restrictions on bond types. For full details, refer to the individual parameter files available on GitHub.

Name	Coverage	Notes
ABEEM		
Yang 1997	C, H, N, O*,+	Parameterised to reproduce HF/STO-3G/MPA charges
Charge2		
Abraham 1982	Br, C, Cl, F, H, I, N, O	Mulliken-derived electronegativities; empirical polarizabilities
Del Re		
Del Re 1958	C, Cl, F, H, N, O+	Electronegativity-based, heuristically tuned to dipole moments
DENR		
Rappe 1991	Br, C, Cl, Cs, F, H, I, K, Li, N, Na, O, P, Rb, S, Si	Derived from experimental atomic IPs and EAs
EEM		
Baekelandt 1991	Al, C, H, N, O, P, Si*	Parameterised to reproduce HF/STO-3G/MPA charges
Bultinck 2002 (CHELPG)	C, F, H, N, O	Parameterised to reproduce B3LYP/6-31G*/CHELPG charges
Bultinck 2002 (Hirshfeld)	C, F, H, N, O	Parameterised to reproduce B3LYP/6-31G*/Hirshfeld charges
Bultinck 2002 (MK)	C, F, H, N, O	Parameterised to reproduce B3LYP/6-31G*/MK charges
Bultinck 2002 (Mulliken)	C, F, H, N, O	Parameterised to reproduce B3LYP/6-31G*/MPA charges

Name	Coverage	Notes
Bultinck 2002 (NPA)	C, F, H, N, O	Parameterised to reproduce B3LYP/6-31G*/NPA charges
Bultinck 2004 (AIM)	C, F, H, N, O	Parameterised to reproduce B3LYP/6-31G*/AIM charges
Geidl 2015 (Cheminf_b3lyp_aim)	Br, C, Cl, F, H, I, N, O, P, S*	Parameterised to reproduce B3LYP/6-311G/AIM charges
Geidl 2015 (Cheminf_b3lyp_mpa)	Br, C, Cl, F, H, I, N, O, P, S*	Parameterised to reproduce B3LYP/6-311G/MPA charges
Geidl 2015 (Cheminf_b3lyp_npa)	Br, C, Cl, F, H, I, N, O, P, S*	Parameterised to reproduce B3LYP/6-311G/NPA charges
Geidl 2015 (Cheminf_hf_aim)	Br, C, Cl, F, H, I, N, O, P, S*	Parameterised to reproduce HF/6-311G/AIM charges
Geidl 2015 (Cheminf_hf_mpa)	Br, C, Cl, F, H, I, N, O, P, S*	Parameterised to reproduce HF/6-311G/MPA charges
Geidl 2015 (Cheminf_hf_npa)	Br, C, Cl, F, H, I, N, O, P, S*	Parameterised to reproduce HF/6-311G/NPA charges
Ionescu 2013 (EX-MPA_6-31Gd_PCM)	C, Ca, H, N, O, S*	Parameterised to reproduce HF/6-31G**/MPA/polarisable-continuum-model charges
Ionescu 2013 (EX-MPA_6-31Gd_gas)	C, Ca, H, N, O, S*	Parameterised to reproduce HF/6-31G**/MPA/gas-phase charges
Ionescu 2013 (EX-NPA_6-31Gd_PCM)	C, Ca, H, N, O, S*	Parameterised to reproduce HF/6-31G**/NPA/polarisable-continuum-model charges
Ionescu 2013 (EX-NPA_6-31Gd_gas)	C, Ca, H, N, O, S*	Parameterised to reproduce HF/6-31G**/NPA/gas-phase charges
Ouyang 2009 (124 calibrated set)	C, H, N, O	Parameterised to reproduce B3LYP/6-31G*/NPA charges

Name	Coverage	Notes
Ouyang 2009 (131 calibrated set)	C, F, H, N, O	Parameterised to reproduce B3LYP/6-31G*/NPA charges
Ouyang 2009 (hybridization-dependent)	C, H, N, O*	Parameterised to reproduce B3LYP/6-31G*/NPA charges
Racek 2016 (ccd2016_mpa)	Br, C, Cl, F, H, N, O, P, S*	Parameterised to reproduce B3LYP/6-311G/MPA charges
Racek 2016 (ccd2016_mpa2)	Br, C, Cl, F, H, N, O, P, S*	Parameterised to reproduce B3LYP/6-311G*/MPA charges
Racek 2016 (ccd2016_npa)	Br, C, Cl, F, H, N, O, P, S*	Parameterised to reproduce B3LYP/6-311G/NPA charges
Racek 2016 (ccd2016_npa2)	Br, C, Cl, F, H, N, O, P, S*	Parameterised to reproduce B3LYP/6-311G*/NPA charges
Svobodova 2007 (cbeg2)	C, H, N, O, S*	Parameterised to reproduce HF/STO-3G/MPA charges
Svobodova 2007 (chal2)	Br, C, Cl, F, H, I, N, O, S*	Parameterised to reproduce HF/STO-3G/MPA charges
Svobodova 2007 (chm2)	Br, C, Cl, F, Fe, H, I, N, O, S, Zn*	Parameterised to reproduce HF/STO-3G/MPA charges
Svobodova 2007 (cmet2)	C, Fe, H, N, O, S, Zn*	Parameterised to reproduce HF/STO-3G/MPA charges
EQeq+C		
Martin-Noble 2015 (ATMO/H-I)	C, H, N, O, Se, Te, V	Bond-order corrections for EQEq, parameterised to reproduce ATMO/Hirshfeld-I charges
Martin-Noble 2015 (MOF/REPEAT)	C, Co, Cu, H, Mg, N, Ni, O, Pd, V, Zn	Bond-order corrections for EQEq, parameterised to reproduce MOF/REPEAT charges
GDAC		
Cho 2001	C, H, N, O, S*	Parameterised to reproduce B3LYP/6-31G** dipole moments and MPA charges

Name	Coverage	Notes
KCM		
Yakovenko 2008 (initial)	C, H, N, O, S*	Parameterised to reproduce MMFF94 charges
MPEOE		
No 1990 (DP1)	C, H, N, O, S*,+	Empirically fitted to dipole (and quadrupole) moments
PEOE		
Gasteiger 1980	Br, C, Cl, F, H, I, N, O, S*	Derived directly from IPs and EAs
QEq		
Rappe 1991	Br, C, Cl, Cs, F, H, I, K, Li, N, Na, O, P, Rb, S, Si	Derived from experimental atomic IPs and EAs
SFKEEM		
Chaves 2006	C, F, H, N, O	Parameterised to reproduce B3LYP/6-31G*/MPA charges
SMP/QEq		
Zhang 2009	Ag, Al, Au, Cu, K, Li, Na, Rb	Fitted to DFT (SVWN) energy derivatives
SQE		
Schindler 2021 (CCD_gen)	Br, C, Cl, F, H, N, O, P, S*,+	Parameterised to reproduce B3LYP/6-311G/NPA charges
Schindler 2021 (DTP_small)	C, H, N, O, S*,+	Parameterised to reproduce B3LYP/6-311G/NPA charges
Schindler 2021 (PUB_pept)	C, H, N, O, S*,+	Parameterised to reproduce B3LYP/6-31G*/NPA charges
SQE+q0		
Schindler 2021 (CCD_gen)	Br, C, Cl, F, H, N, O, P, S*,+	Parameterised to reproduce B3LYP/6-311G/NPA charges

Name	Coverage	Notes
Schindler 2021 (DTP_small)	C, H, N, O, S*,+	Parameterised to reproduce B3LYP/6-311G/NPA charges
Schindler 2021 (PUB_pept)	C, H, N, O, S*,+	Parameterised to reproduce B3LYP/6-31G*/NPA charges
SQE+qp		
Schindler 2021 (CCD_gen)	Br, C, Cl, F, H, N, O, P, S*,+	Parameterised to reproduce B3LYP/6-311G/NPA charges
Schindler 2021 (DTP_small)	C, H, N, O, S*,+	Parameterised to reproduce B3LYP/6-311G/NPA charges
Schindler 2021 (PUB_pept)	C, H, N, O, S*,+	Parameterised to reproduce B3LYP/6-31G*/NPA charges
TSEF		
Rappe 1991	Br, C, Cl, Cs, F, H, I, K, Li, N, Na, O, P, Rb, S, Si	Derived from experimental atomic IPs and EAs

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